2014-1373, -1399

United States Court of Appeals for the Federal Circuit

KANEKA CORPORATION, A Japanese Corporation,

Plaintiff-Appellant,

v.

XIAMEN KINGDOMWAY GROUP COMPANY, a Chinese Corporation, PACIFIC RAINBOW INTERNATIONAL INC., a California Corporation, and SHENZHOU BIOLOGY AND TECHNOLOGY CO., LTD., a Chinese Corporation,

Defendants-Appellees.

Appeals from the United States District Court for the Central District of California in No. 2:11-v-02389-MRP-SS, Senior Judge Mariana R. Pfaelzer.

CORRECTED NON-CONFIDENTIAL BRIEF FOR PLAINTIFF-APPELLANT

KEITH D. NOWAK
nowak@clm.com
CARTER LEDYARD & MILBURN LLP
2 Wall Street
New York, NY 10005
(212) 732-3200

ROBERT M. BOWICK, JR.
rbowick@raleybowick.com
RALEY & BOWICK, LLP
1800 Augusta Drive, Suite 300
Houston, Texas 77057
(713) 429-8050

Counsel for Plaintiff-Appellant Kaneka Corporation

Filed June 3, 2014
Corrected: June 19, 2014

CERTIFICATE OF INTEREST

Pursuant to Federal Circuit Rule 47-4, counsel for the Plaintiff-Appellant Kaneka Corporation certifies the following:

1. The full name of every party or amicus represented by me is:

   Kaneka Corporation.

2. Kaneka Corporation is the real party in interest.

3. No publicly held companies hold more than 10% of the stock of Kaneka Corporation.

4. The names of all law firms and the partners or associates that appeared for Kaneka Corporation in the District Court, or are expected to appear in this Court, are:

   Keith D. Nowak of Carter Ledyard & Milburn LLP,

   Robert M. Bowick Jr. of Raley and Bowick LLP,

   Adrian M. Pruetz and Charles Christian Koole of Glaser Weil Fink Jacobs Howard Avchen and Shapiro LLP;

   Victor L. George and Wayne C. Smith of The Law Offices of Victor L. George,

   Dariush G. Adli of Adli Law Group PC,

   Dave Deonarine and Raymond K. Chan of Procopio Cory Hargreaves & Savitch LLP;

   Benjamin C. Deming of DNL Zito.

Dated: June 3, 2014

Respectfully submitted:

By: /s/ Keith D. Nowak

Keith D. Nowak
Counsel for Plaintiff-Appellant
Kaneka Corporation

TABLE OF CONTENTS

Page

CONFIDENTIAL MATERIAL OMITTED

The material omitted on pages 13, 37, and 45, and Addendum pages A14052 -60, and A14070-78 describes aspects of Defendants-Appellees' confidential, proprietary, and trade secret processes for producing the chemical coenzyme Q10 on an industrial scale.

TABLE OF AUTHORITIES

Page(s)

FEDERAL CASES

STATUTES AND RULES

OTHER AUTHORITIES

I. STATEMENT OF RELATED CASES

Pursuant to Federal Circuit Rule 47.5, Counsel for Plaintiff-Appellee Kaneka Corporation certifies that:

1. No other appeal in or from the underlying civil action in this case has been previously before this court or any other appellate court.

2. The case of *Zhejiang Medicine Co. Ltd. and ZMC-USA LLC v. Kaneka Corporation*, Civil Action No. 4:11-CV-1052 (VDG), United States District Court for the Southern District of Texas, Houston Division, may be directly affected by this Court's decision.

II. STATEMENT OF JURISDICTION

The District Court's jurisdiction arose under 28 U.S.C. § 1338 based upon the asserted claims of patent infringement against Xiamen Kingdomway Group Company, Pacific Rainbow International, Inc., and Shenzhou Biology and Technology Co. Ltd.

Because the District Court's jurisdiction arose under § 1338, this Court has appellate jurisdiction. 28 U.S.C. § 1295(a)(1).

This appeal was timely filed in accordance with 28 U.S.C. § 2107 and Fed.R.App.P 4(a).

This is an appeal from: (1) a final judgment, dated March 27, 2014, which implemented two orders which (a) granted in part Xiamen Kingdomway Group Company's Motion for Summary Judgment of Non-infringement of U.S. Patent No. 7,910,340 and (b) granted in part Shenzhou Biology and Technology Co. Ltd.'s Motion for Summary Judgment of Non-infringement of U.S. Patent No. 7,910,340, and from (2) the District Court's Claim Construction Order dated July 24, 2013.

III. STATEMENT OF ISSUES FOR REVIEW

1. Did the District Court err in its construction of the term "inert gas atmosphere" in independent claims 1 and 11 of U.S. Patent No. 7,910,340 (the "'340 patent"), by limiting it to "a gas atmosphere that is free or substantially free of oxygen and reactive gases"? (A3578)

2. Did the District Court err in its construction of the term "sealed tank" in independent claims 22 and 33 of the '340 patent by limiting it to "a tank that is closed to prevent the entry or exit of materials"? (A3579)

3. Did the District Court err in its construction of the method step "culturing reduced coenzyme Q_{10} producing microorganisms . . . to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10}" in independent claims 1, 11, 22 and 33 of the '340 patent by limiting it to "culturing reduced coenzyme Q10 producing microorganisms to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzyme Q_{10} at a time prior to the extraction, oxidation, or disruption steps and as determined by the assay described at Col. 5:8-43, and Example 1 of the '340 patent"? (A3583)

4. Did the District Court err in its construction of the method step "oxidizing **thus-obtained** reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" in independent claims 1 and 22 of the '340 patent by limiting it to "actively converting all or substantially all of the reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a step **before** beginning the extraction step" and err in its construction of the method step "oxidizing **the extracted** reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" in independent claims 11 and 33 of the '340 patent by limiting it to "actively converting all or substantially all of the extracted reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a separate step **after** the extraction step has been performed"? (A3585-3586) (*emphasis added)*

IV. STATEMENT OF THE CASE

On March 22, 2011, Kaneka filed an original complaint against Defendant-Appellee Shenzhou Biology & Technology Co. Ltd. ("Shenzhou") and Defendants-Appellees Xiamen Kingdomway Group Co., and Pacific Rainbow International Inc. (collectively "XKGC") asserting infringement of U.S. Patent No. 7,910,340 (the "'340 Patent"). (A82-93) XKGC and Shenzhou (collectively "Defendants") answered and counterclaimed, alleging non-infringement, invalidity, and unenforceability of the '340 Patent. (A1123-1153; A1171-1185) XKGC additionally counterclaimed against Kaneka for tortious interference with prospective business relationships (Third Counterclaim); trade libel (Fourth and Fifth Counterclaims); libel (Sixth and Seventh Counterclaims); unfair competition under the Lanham Act (Eighth Counterclaim); and the California Business Code (Ninth Counterclaim) "counterclaims 3-9". (A1123-1153)

On July 24, 2013, the District Court construed the four claim terms at issue in this appeal (A3571-3587), following a *Markman* hearing held on July 11, 2013. (*See* A3567)

On August 27, 2013, Shenzhou filed a motion for summary judgment of non-infringement of the '340 patent based upon the District Court's claim construction. (A3589-5204)

On September 17, 2013, XKGC filed a motion for summary judgment of non-infringement of the '340 patent based upon the District Court's claim construction. (A7990-7995)

On November 12, 2013, Kaneka filed a motion for summary judgment on XKGC counterclaims 3-9 and a motion for summary judgment of patent validity and enforceability. (A10472-10474; A10475-10477)

On December 6, 2013, the District Court granted in part XKGC's, and Shenzhou's motions for summary judgment of non-infringement. (A14044-14061; A14062-10479)

On February 24, 2014, the District Court granted Kaneka's motion for summary judgment on XKGC's counterclaims 3-9. (A4-15)

Also on February 24, 2014, the District Court denied Kaneka's motion for summary judgment of patent validity and enforceability as moot in light of its summary judgment of non-infringement. (A14081-14084) The District Court's orders on summary judgment resolved all claims and counterclaims pending in the proceeding. (A4-15; A14044-14061; A14062-14079; A14081-14084)

On March 12, 2014, Kaneka filed a Notice of Appeal from: (1) the two Orders of the District Court, dated December 6, 2013, which: (a) granted in part XKGC's Motion for Summary Judgment of Non-infringement of the '340 Patent (A14046-14061) and (b) granted in part Shenzhou's Motion for Summary

Judgment of Non-infringement of the ‘340 Patent (A14064-14079), and (2) the District Court's Claim Construction Order dated July 24, 2013. (A3571-3587) The Notice of Appeal was filed at that time because, on February 25, 2014, the District Court entered an Order granting Kaneka’s Motion for Summary Judgment Dismissing XKGC’s remaining counterclaims. (A4-15) The District Court’s February 25 Order resolved all remaining issues in the proceeding, and Kaneka believed the February 24 Order to be a Final Judgment from which an appeal could be taken pursuant to 28 U.S.C. § 1295. Kaneka’s Notice of Appeal dated March 12, 2014 was assigned Case No. 12-1373.

Subsequently, on March 27, 2014, a month after Kaneka filed its first Notice of Appeal, the District Court formerly entered a Final Judgment (A1-3) implementing the Court's Orders dated December 6, 2013 (A14046-14061), (A14064-14079), and February 24, 2014. (A14081-14084) Therefore, on April 2, 2014, Kaneka filed a second Notice of Appeal from the Judgment, which was assigned Case No. 14-1399.

On April 18, 2014, Kaneka filed a motion with this Court to consolidate the two appeals which was granted on May 12, 2014.

V. STATEMENT OF THE FACTS

A. Introduction

This case involves an industrial process for producing coenzyme Q_{10} ("CoQ_{10}") covered by the claims of the '340 patent.

CoQ_{10} is a substance that is naturally found in every cell of the human body. Human cells use CoQ_{10} to produce the energy needed for cell growth and maintenance. CoQ_{10} is produced in cells by biosynthesis, and is acquired by supplementation and in small amounts from diet. CoQ_{10} is an essential component of the electron transport chain within the mitochondria of each cell. It functions as an anti-oxidant, protecting the body from damage caused by harmful molecules, and prevents oxidative damage to lipids, proteins, and DNA. CoQ_{10} is found in the highest concentrations in parts of the body which have the highest metabolic energy requirements, such as the heart, kidney, liver and skeletal muscle.

CoQ_{10} exists in two forms: (1) reduced and (2) oxidized. Reduced refers to the chemical composition of CoQ_{10} that has extra electrons. After reduced CoQ_{10} gives up the extra electrons, it becomes oxidized CoQ_{10}. CoQ_{10} continuously gains and gives up electrons in a reduction-oxidation cycle. This continuous electron-exchange-cycle facilitates the transfer of energy through the human body. Kaneka's '340 patent claims a process for producing oxidized

coenzyme Q_{10} ("oxidized CoQ_{10}"). The parties in the litigation produce oxidized CoQ_{10} and market and sell the finished product as a dietary supplement. Kaneka produces oxidized CoQ_{10} in the United States and Japan and the Defendants produce oxidized CoQ_{10} in China.

Kaneka has been producing CoQ_{10} since 1977. Beginning in 1998, Kaneka began work on a new process for manufacturing CoQ_{10}. In June 2001, while screening various microorganisms to be used in Kaneka's new manufacturing process, the inventors of the '340 patent discovered that—contrary to conventional wisdom—the microorganisms were producing CoQ_{10} in reduced, rather than oxidized form. Based in part on this discovery, the inventors of the '340 patent developed a patented process covered by the '340 patent for industrial scale manufacturing of oxidized CoQ_{10} that was both safe and efficient. Kaneka filed its first patent application in Japan on December 27, 2001. On October 31, 2007, Kaneka's '340 patent was filed in the United States as a divisional of a patent filed under the Patent Cooperation Treaty (PCT), and claimed priority to the Japanese patent application. Kaneka's '340 patent issued on March 22, 2011.

B. The ‘340 Patent

The parent application for the ‘340 patent, U.S. Patent Application No. 10/500,249, was filed on November 3, 2004, based on PCT application PCT/JP02/13766, which was filed on December 27, 2002. As filed, the specification in the parent application described a production process for producing both reduced CoQ_{10} and oxidized CoQ_{10}. Indeed, the vast majority of the specification describes the production of reduced CoQ_{10} with only selected portions of the specification describing the production of oxidized CoQ_{10} as discussed in greater detail below. The parent application included a set of claims directed to the production of reduced CoQ_{10} and a set of claims directed to the production of oxidized CoQ_{10}. During prosecution in the U.S. Patent Office, the Examiner issued a restriction requirement which required the applicant, Kaneka, to select either the reduced CoQ_{10} claim set or the oxidized CoQ_{10} claim set for further prosecution. (A550-555) Kaneka selected the reduced CoQ_{10} claims for further prosecution, which claims were subsequently rejected by the U.S. Patent Office and abandoned by Kaneka.[1]

Kaneka then filed, on October 31, 2007, divisional application serial no. 11/981,181 to prosecute the oxidized CoQ_{10} claim set, which application issued as the ‘340 patent on March 22, 2011. Therefore although the ‘340 patent

[1] Both sets of claims, oxidized and reduced, were allowed in Europe in European Patent No. EP 1 466 983 B1

specification describes both the production of reduced and oxidized CoQ_{10}, all claims in the '340 patent are directed to the production of oxidized CoQ_{10}.

C. <u>The Patented Process</u>

The independent claims of the '340 patent describe four different processes for producing oxidized CoQ_{10}. The four disputed claim terms, all in the independent claims, were construed in the District Court's Claim Construction Order (A3571-3587) The claim terms are underlined and numbered in Table 1 on the following page:

TABLE 1

<table>
<tr><th>CLAIM 1</th><th>CLAIM 22</th><th>CLAIM 11</th><th>CLAIM 33</th></tr>
<tr><td colspan="4">[3] Culturing reduced coenzyme Q_{10} producing microorganisms to obtain microbial cells containing reduced CoQ_{10} at a ratio of not less than 70 mole% among the entire coenzymes Q_{10}.</td></tr>
<tr><td colspan="2">Disrupting the microbial Cells to obtain reduced coenzyme Q_{10}.</td><td rowspan="2">Extracting the reduced coenzymes Q_{10} by an organic solvent under an [1] Inert Gas Atmosphere</td><td rowspan="2">Extracting the reduced coenzyme Q_{10} by an organic solvent in a [2] Sealed Tank</td></tr>
<tr><td colspan="2">[4] Oxidizing thus obtained reduced CoQ_{10} to oxidized coenzyme Q_{10}.</td></tr>
<tr><td>Extracting the oxidized coenzyme Q_{10} by an organic solvent under an [1] Inert Gas Atmosphere</td><td>Extracting the oxidized coenzyme Q_{10} by an organic solvent in a [2] Sealed Tank</td><td colspan="2">[4] Oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}.</td></tr>
</table>

Production of oxidized CoQ_{10} requires culturing, disrupting, extracting and oxidizing. Culturing must occur first but the remaining steps are not in any particular order as shown by the independent claims and explained in greater detail below. Examples of microorganisms capable of being cultured to produce reduced CoQ_{10} at a ratio of not less than 70 mole % are set forth in Table 1 of the '340 patent. (A75)

The process for culturing the microorganisms is described in the patent at Col. 7:66-67-Col. 8:1-65 (A70), and the goal of the process is to obtain reduced CoQ_{10} at a ratio of not less than 70 mole % among the entire $CoQ_{10.}$ (Col. 8:66-67, Col. 9:6) (A70-71) The ratio of reduced CoQ_{10} continues to increase during culturing until the microorganism's food source is depleted. The culture is completed when a desired amount of reduced CoQ_{10} is produced. (Col. 8:54-55) (A70) Culturing is also carried out aerobically *i.e.*, oxygen is supplied during the culturing step (Col. 8:58-60) (A70) Therefore, oxidation of the reduced CoQ_{10} does occur during the culturing step, but the amount of reduced CoQ_{10} will continue to increase with a sufficient food source.

Disrupting the microbial cells can be carried out to the extent that the surface structure, such as the cell wall is broken (Col. 9:22-24), and disruption and extraction can be carried out at the same time. (Col. 9:19-20)

Confidential Material Redacted

(A71) The disruption method can include a physical treatment (i.e. mechanical disruption), a chemical treatment, an enzyme treatment as well as a heating treatment, etc. (Col. 9:33-63) (A71)

Extraction is performed by mixing the microbial cells and the disrupted product thereof with an organic solvent. (Col. 17:1-7) (A75) The patent identifies a number of generic organic solvents that can be used. (*see* Col. 10:50-53) (A71) In actual production Kaneka uses hexane as the organic solvent. Organic solvents are highly flammable, including hexane, and safety precautions must be taken when working with organic solvents.

In the oxidation process, the reduced CoQ_{10}, produced from culturing the microorganisms is oxidized to obtain oxidized CoQ_{10}. [redacted]

The obtained oxidized CoQ_{10} is purified by column chromatography or the like and subjected to a crystallization operation to produce high purity oxidized CoQ_{10} crystals, which comprise the final product. (Col. 17:25-30) (A75)

D. The Proceedings Below

Kaneka filed its complaint in the Central District of California on March 22, 2011 ("the California Litigation") alleging infringement of the '340 patent against Defendants Maypro Industries Inc., Mitsubishi Gas Chemical Company Inc., Pacific Rainbow International Inc., Shenzhou, XKGC and ZMC-USA LLC and Zhejiang Medicine Co. Ltd. (collectively "ZMC") (A82-93) On that same day, ZMC filed for declaratory relief against Kaneka in the Southern District of Texas alleging that the '340 patent was invalid and not infringed ("the Texas Litigation"). The California District Court on June 23, 2011 transferred the case against ZMC to the Southern District of Texas. (A1019-1020, A 1030-1031)

On June 17, 2011, Kaneka filed a complaint in The International Trade Commission against all of the Defendants ("the ITC Litigation"). In view of the ITC Litigation, the California District Court granted the parties' motion to stay the California Litigation on August 2, 2011. (A1056-1059) The stay was lifted in the California Litigation on February 7, 2013, after the conclusion of the ITC

Litigation. Both Mitsubishi Gas Chemical Company Inc. and Maypro Industries Inc. were dismissed from the California Litigation by Stipulation. (A3568-3570, A10597-10598) The Texas Litigation was not stayed and a Claim Construction Order was entered in that case on August 23, 2012. (A3297-3359) The ITC Litigation also included a claim construction analysis with a final decision on claim construction definitions included in the ALJ's Initial Determination of September 27, 2012. (A5308-5351) A Claim Construction Order was entered in the California Litigation on July 24, 2012. (A3571-3587)

E. The Texas Court's and ALJ's Claim Constructions

Most, but not all, of the claim terms to be considered in this appeal were previously construed in the Texas Litigation and the ITC Litigation. The California District Court considered both prior claim constructions and adopted, in part, the reasoning from the Texas and ITC Litigations for some of the claim terms, as discussed in greater detail below. Table II below sets forth the prior claim constructions as well as the claim construction adopted by the California District Court.

TABLE II

Claim Terms	Texas Court's Construction (August 23, 2012)	ITC Construction (September 27, 2012)	California Court's Construction (July 24, 2013)
1) "inert gas atmosphere" Claims 1, 11	"a gas atmosphere that is substantially free of reactive gases." (A3332-3337)	"an atmosphere of inert gas (such as nitrogen, carbon dioxide, helium, argon or hydrogen) that is free or substantially free of oxygen." (A5336)	"a gas atmosphere that is free or substantially free of oxygen and reactive gases." (A3578)
2) "sealed tank" Claims 22, 33	"a tank that prevents exposure of its content to the atmosphere" (A3338-3342)	"a tank that is closed to prevent the entry or exit of materials." (A5346)	"a tank that is closed to prevent the entry or exit of materials." (A3579)
3) "culturing reduced coenzyme Q_{10} producing micro-organisms … to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the	Term not disputed during Texas claim construction	The ALJ did not construe this exact term. However, the ALJ did find that the claims are not limited by the method at Col. 5:8-43, (ITC Decision at page 16) and also decided that "The sampling point to determine whether or not the 70 mole % ration limitation is satisfied is at the end of culturing, which is the end of	"culturing reduced coenzyme Q_{10} producing microorganisms to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzyme Q_{10} at a time prior to the extraction, oxidation or disruption steps and as determined by

Claim Terms	Texas Court's Construction (August 23, 2012)	ITC Construction (September 27, 2012)	California Court's Construction (July 24, 2013)
entire coenzymes Q_{10}" Claims 1, 11, 22, 23		fermentation." (A5562-5563)	the assay described at Col. 5:8-43, and Example 1 of the '340 patent." (A3583)
4) "oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" Claims 11, 22 and "oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" Claims 11, 33	"oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" and "oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}". (A3328-3331; A3349-3352)	Term not disputed during ITC claim construction	"actively converting all or substantially all of the reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a step before beginning the extraction step" and "actively converting all or substantially all of the extracted reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a separate step after the extraction step has been performed" (A3585-3586)

1) Reasoning of The Texas Federal District Court

i) Inert Gas Atmosphere

In the Texas Litigation Kaneka argued that "extracting – under an inert gas atmosphere" should be defined as "extracting – under a gas atmosphere that is less readily reactive with the organic solvent". (A3332-3337) Kaneka relied on two sections of the patent specification in support of its position:

> On the industrial scale, complete oxygen elimination is very difficult to be achieved and, furthermore, fairly long periods of time are required for individual operations, unlike laboratory scale production, so that residual oxygen exerts a great adverse effect. (Col. 10:60-64)
>
> Incidentally, it is not necessary to carry out the recovery of oxidized coenzyme Q_{10} under the condition that reduced coenzyme Q_{10} is protected from an oxidation reaction, which is recommended for the recovery of reduced coenzyme Q_{10}, and the recovery may be carried out in consideration of general safe operation and the like. (Col. 17:20-25) (A3333)

Kaneka submitted that because the specification states that "complete oxygen elimination is very difficult to be achieved" the term "inert gas atmosphere" should be interpreted as meaning an atmosphere that allows the presence of some oxygen even though oxygen is not an inert gas. Kaneka also contended that because the patent specification discusses the recovery of oxidized Q_{10}, "in consideration of general safe operation", the term "under an inert gas atmosphere" should be interpreted in light of what constitutes safety concerns when working with a flammable organic solvent. (A3334-3335)

ZMC, the Defendant in the Texas Litigation argued that "extracting – under an inert gas atmosphere should be defined as "extracting – where the extraction takes place in an atmosphere of a chemically inert gas." (A3332) ZMC pointed to the section in the specification which provided:

> As 'the condition that reduced coenzyme Q_{10} is protected from an oxidation reaction' means, for example, a deoxygenized atmosphere (an atmosphere of an inert gas such as nitrogen gas, carbon dioxide gas, helium gas, argon gas or hydrogen gas, reduced pressure, a boiling condition);… (Col. 16, :36-39) (A3335)

Based on this statement in the specification, ZMC asserted that the patent teaches that an inert gas atmosphere is completely deoxygenized.

The Texas Court did not accept ZMC's position on "inert gas atmosphere" stating that:

> The patent never defines an inert gas atmosphere as one that is completely deoxygenized. Instead the patent specification provides examples of a deoxygenized atmosphere, such as 'an atmosphere of an inert gas, such as nitrogen gas, carbon dioxide gas, helium gas, argon gas. (A3336)

The Texas Court decided that "extracting – under an inert gas atmosphere" means "extracting – under a gas atmosphere that is substantially free of reactive gases" and further stated that "the term 'substantially free of reactive gases" better describes an inert gas atmosphere in accordance with the patent specifications safety concerns. (A3337)

Although not specifically highlighted by the Texas Court it is important to note that the specification section relied on by ZMC (Col. 16:36-39) (A74) is specifically limited to protecting **reduced** coenzyme Q_{10} from an oxidation reaction by using a deoxygenized atmosphere. As set forth above, the patent specification covers the production of both reduced and oxidized Q_{10}, but the claims at issue in this case cover only oxidized Q_{10}. Protecting oxidized Q_{10} from an oxidizing reaction by use of a deoxygenized atmosphere does not make sense because the objective of the patented process is to produce oxidized Q_{10}.

ii) Sealed Tank

In the Texas Litigation, Kaneka proposed that "sealed tank" be defined as "extracting the oxidized CoQ_{10} by an organic solvent in a tank that substantially prevents direct exposure of its contents to the atmosphere." (A3338) The basis for Kaneka's proposed definition was threefold (1) one skilled in the art would interpret "in a sealed tank" with respect to safety concerns, (2) Fig. 1 in the patent does not show a completely sealed tank and (3) in the context of industrial scale production, tanks necessarily contain vents or release valves. (A3339)

ZMC argued that the term "sealed tank" be defined as a tank in a sealed state to prevent the entry or escape of liquids or gases during the extraction process. (A3340) The Texas Court rejected ZMC's proposed construction

because it relied on extrinsic evidence from other definitions of sealed tanks and from inventor testimony. The Texas Court accepted Kaneka's reasoning, based on the three points Kaneka offered in support, but simplified Kaneka's proposed definition to find that "sealed tank" means "extracting the oxidized coenzyme Q_{10} by an organic solvent in a tank that prevents exposure of its contents to the atmosphere." (A3341-3342)

iii) Culturing to Obtain 70 Mole %

The Texas Court did not define claim term 3 as it was not in dispute in Texas.

iv) Oxidizing Reduced Co Q_{10}

This claim term covered the step of oxidizing reduced CoQ_{10} to obtain oxidized CoQ_{10}. In claims 1 and 22, the claim language is "oxidizing *thus-obtained* reduced coenzyme –" and in claims 11 and 33, the claim language is "oxidizing *the extracted* reduced coenzyme Q_{10} –".

ZMC argued that the claim language for all four independent claims should be construed to mean "in a separate step, oxidizing all or substantially all of the reduced coenzyme Q_{10} obtained from the disruption step before beginning the extraction step" (A3329) which is the same construction proposed by the Defendants in the California District Court.

The Texas Court rejected the conditions proposed by both Kaneka and ZMC stating:

> However, these conditions are not present, or even suggested by, the patent claims, specification or prosecution history. There is no language referring to the rate of oxidization, or an increase in the rate of oxidization. Likewise, there is no language stating that oxidization must occur in a separate step, or that all or substantially all of the reduced coenzyme Q10 obtained from extraction be oxidized. Although ZMC argues that the patent makes little sense unless it includes ZMC's conditions, ZMC has failed to present any evidence showing that its conditions are necessary. For example, ZMC has failed to show that the claimed processes will produce oxidized CoQ10 only if extraction is a separate step from oxidization. ZMC has also failed to show that the claimed processes will produce oxidized CoQ10 only if "all or substantially all" of the extracted reduced CoQ10 is oxidized. Furthermore, although the processes in Claims 11 and 33 are for producing oxidized CoQ10, the fact that oxidized CoQ10 is an end product does not mean that "all or substantially all" of the extracted reduced CoQ10 must be oxidized. Even if only a small part of the extracted reduced CoQ10 is oxidized, the processes will nonetheless result in oxidized CoQ10. The Court declines to adopt either of the proposed constructions, because they both import additional conditions into the patent. (A3351)

Accordingly, the Texas Court concluded this claim term did not require construction.

2) Reasoning of the ALJ in the ITC litigation

The claim construction by ALJ Rogers in the ITC litigation does not have any preclusive effect on this Court or the California District Court. *Texas Instr. v. Cypress Semiconductor Corp.*, 90F. 3d 1558, 1569 (Fed. Cir. 1996). In *Texas*

Instruments, the Federal Circuit ruled that ITC decisions, as well as Federal Circuit decisions on appeal from the ITC, including claim construction decisions, have no preclusive effect in actions involving identical patent claims. However, because the California District Court, in some instances (*see* below), relied on the reasoning of the ALJ in the ITC litigation "in its entirety", Kaneka addresses the reasoning of the ALJ herein.

i) Inert Gas Atmosphere

Kaneka proposed the same construction in the ITC Litigation that it had proposed in the Texas Litigation and based its proposed construction on the same arguments it had made in Texas. (A5333-5334)

The ITC Respondents proposed that "inert gas atmosphere" means "an atmosphere of inert gas that is free or substantially free of oxygen" (A5334) and relied on the same portion of the specification at Col. 16:32-39 that ZMC had relied on in the Texas Litigation, *i.e.*,

> As the condition that reduced coenzyme Q10 is protected from an oxidation reaction means, for example, a deoxygenized atmosphere (an atmosphere of inert gas such as nitrogen gas, carbon dioxide gas, helium gas, argon gas…..)

As set forth above, this section of the specification is specifically limited to reduced CoQ10 and does not apply to the recovery of oxidized CoQ10 as there is no need to protect oxidized CoQ10 from oxidation. Nonetheless, ALJ

Rogers concluded that "inert gas atmosphere" means "an atmosphere of inert gas (such as nitrogen, carbon dioxide, helium, argon or hydrogen) that is free or substantially free of oxygen". The ALJ incorrectly relied on Col. 16:32-39 of the specification in which *reduced* $CoQ_{10,}$ not oxidized $CoQ_{10,}$ is protected from oxidation in a deoxygenized atmosphere. (A5336)

ii) Sealed Tank

Kaneka proposed the same construction in the ITC Litigation for this claim term that it proposed in the Texas Litigation, *i.e.*, that a "sealed tank" meant "a tank that substantially prevents direct exposure of its contents to the atmosphere." (A5341) In support of its proposed construction, Kaneka argued that in the production of CoQ_{10}, the release of volatile hydrocarbons into the atmosphere surrounding the extraction tank must be avoided for safety reasons and the uncontrolled entry of materials into the extraction tank must be avoided to prevent contamination. Kaneka contended that the purpose of using a "sealed tank" is to meet these goals. Kaneka further argued that its construction takes into account the commercial reality of extracting fermented products using organic solvents, including the use of a venting device for relieving pressure in the tank while still preventing escape of solvent vapors to the atmosphere. (A5341)

Kaneka also pointed to Figure 1 in the '340 patent as showing that the tanks are not sealed but provide for the transfer of material between the tanks. (A5341-5342)

Respondents relied on extrinsic evidence, *i.e.* the dictionary definition of "seal" as a "tight and perfect closure" to propose that "sealed tank" means "a tank that has been closed off to protect the contents of the tank from exposure to air and otherwise prevent the entry or escape of gases during the extraction process." (A5343)

The ALJ concluded that "sealed tank" meant "a tank that is closed to prevent the entry or exit of material," relying on the extrinsic evidence of a dictionary definition (A5346) and failing to take note of the intrinsic evidence available in the specification of the '340 patent in order to arrive at an appropriate claim construction.

iii) Culturing to Obtain 70 Mole %

As set forth above, the ALJ did not construe this exact term, but did find that the claims were not limited by the culturing method of Col. 5:9-43 in the '340 patent specification. (A5317) The ALJ also decided that the sampling point to determine whether or not the 70 mole % ratio limitation is satisfied is at the end of fermentation. (A5562-5563) The ALJ arrived at this conclusion without any support in the specification or file history, but relied on an alleged order in the production steps supposedly required in the claim language.

(A5562-5563) The District Court followed this reasoning in error, as set forth below.

iv) Oxidizing Reduced Co Q_{10}

This claim term was not disputed during the ITC litigation.

F. California District Court's Claim Construction

On May 15, 2013, the California Court entered a Markman Scheduling Order (A1109-1110) and the Markman Hearing was conducted on July 11, 2013. The claim terms at issue and the parties proposed claim constructions are set forth in Table III.

Table III

Claim Nos.	Claim Terms	Kaneka's Construction	Defendant's Construction
1-21, 29, 30	1) "inert gas atmosphere"	a gas atmosphere that is less readily reactive with the organic solvent	an atmosphere of inert gas (such as nitrogen, carbon dioxide, helium, argon or hydrogen) that is free or substantially free of oxygen
22-45	2) "sealed tank"	a tank that substantially prevents direct exposure of its contents to the atmosphere	a tank that is closed to prevent the entry or exit of materials
1-45	3) "culturing reduced coenzyme Q_{10} producing micro-organisms … to obtain	No construction necessary. Alternatively, culturing (i.e., growing of living	culturing reduced coenzyme Q_{10} producing micro-organisms to obtain

Claim Nos.	Claim Terms	Kaneka's Construction	Defendant's Construction
	microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10}"	cells in a controlled artificial environment) reduced coenzyme Q_{10} (i.e., class of 2,3-Dimethoxy-5-methyl quinones, semiquinones, and quinols with ten isoprene units substituted at the C-6 position), producing microorganisms to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10} (reduced coenzyme Q_{10} comprises $\geq$ 70 mole % of the total coenzyme Q_{10}, i.e., reduced coenzyme Q_{10} plus oxidized coenzyme Q_{10}).	microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzyme Q_{10} as determined by the assay described at Col. 5, l. 8 to l. 43, and Example 1 of the '340 patent.
1-45	4) "oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" and "oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}"	No construction necessary, (i.e., "oxidizing thus obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" and" the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}".	Actively converting all or substantially all of the reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a step before beginning the extraction step has been performed.

(A3577, A3579, A3580, A3584)

The Court issued its Claim Construction Order on July 24, 2013. (A3571-3587) The reasoning of the Court with respect to each disputed claim term is set forth below.

1) Inert Gas Atmosphere

The Court found that "inert gas atmosphere" means "a gas atmosphere that is free or substantially free of oxygen and reactive bases". (A3578) However, in the Court's Order Granting in Part Defendant Shenzhou Biology & Technology Co Ltd.'s Motion for Summary Judgment of Non-Infringement (A14062-14079), the Court appeared to remove "substantially free" from the definition. The Court rejected Kaneka's proposition to construe the term "inert gas atmosphere" in light of safety considerations and the argument that the presence of some oxygen in the extraction tank would fall within the definition of "substantially free". Instead the Court stated, "the term 'free' in this usage is something not subject to a given condition – here the condition of the presence of oxygen". (A14074) In other words, it appears that the Court, when applying its definition, removed "substantially free" from the definition and required that an "inert gas atmosphere" means an atmosphere free of all oxygen. This is not surprising as the Court in its Claim Construction Order relied heavily on the same section of the patent specification in which recovery of *reduced* CoQ_{10} requires a deoxygenized atmosphere. (A3577-3578) The Court further found

that the "Plaintiff has acted as its own lexicographer in its specification by defining an environment for protecting against an oxidation reaction by examples including a deoxygenized atmosphere." (A3578) As set forth above, and as described in greater detail below, the section of the specification relied on by the Court is limited to the production of reduced CoQ_{10} and does not apply to oxidized CoQ_{10}.

2) Sealed Tank

In its one-page of reasoning with respect to this disputed claim term, the Court found that "sealed tank" means "a tank that is closed to prevent the entry or exit of materials", the same definition proposed by Defendants. (A3579) The Court also made it clear that it had adopted "the reasoning presented in the ITC Proceeding with respect to the claim construction of the term 'sealed tank' in its entirety". (A3579) Kaneka's argument that "sealed tank" should be considered with respect to safety considerations was rejected in its entirety.

3) Culturing To Obtain 70 Mole %

For this claim term the District Court found that "culturing reduced coenzyme Q_{10} producing microorganisms . . . to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzyme Q_{10}" means "culturing reduced coenzyme Q_{10} producing microorganisms to obtain microbial cells containing reduced coenzyme Q_{10} at a

ratio of not less than 70 mole % among the entire coenzyme Q_{10} at a time prior to the extraction, oxidation, or disruption steps and as determined by the assay described at Col. 5:8-43, and Example 1 of the '340 patent." (A3583)

Kaneka had proposed that no construction was necessary for this claim term. Defendants had proposed a construction limiting the method of measuring 70 mole % to the specific example in the patent, a construction rejected by the ALJ in the ITC Litigation. The District Court's construction went beyond any definition proposed by the parties and added a new limitation to Defendants' proposed construction requiring that the 70 mole % amount must be measured at a specific time in the production process. (A3580-3582)

Nothing in the specification or file history says anything about the timing point in the process at which to measure for 70 mole %. The District Court in fact conceded that "[t]he claims do not explicitly state a timing requirement for the mole percent determination . . . ." (A3581) However, the District Court concluded that the steps in the production process must be performed in a specific order, that other steps of the claim affect the mole % amount and therefore the mole percent of reduced CoQ_{10} "must be determined at a time prior to the execution of any of the subsequent steps of the claims." (A3582) The premise of production steps being performed in a specific order relied on by the

District Court is refuted below and thus the District Courts conclusion was in error.

4) Oxidizing Reduced CoQ_{10}

For this claim term the District Court found that "oxidizing *thus-obtained* reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" means "actively converting all or substantially all of the reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a step *before* beginning the extraction step" and found that "oxidizing *the extracted* reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" means "actively converting all or substantially all of extracted reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a separate step *after* the extraction step has been performed". (A3585-3586)

Again, the District Court adopted the reasoning presented in the ITC Proceeding with respect to the claim construction of the order of the steps. (A3584-3585) The District Court also added "actively converting" to the claim construction based on an example in the specification. (A3585) The language relied on by the District Court with respect to the use of an oxidizing agent for "actively converting" reads as follows:

> The above-mentioned oxidation **may** be carried out by, **for example**, mixing reduced coenzyme Q_{10} (preferably an aqueous suspension of the microbial cells or disrupted product thereof containing reduced coenzyme Q_{10}, an extract

> containing reduced coenzyme Q_{10}, or the like) with a oxidizing agent (*e.g.*, manganese dioxide or the like) and then, for example, oxidizing the mixture at room temperature (*e.g.*, 30º C.) for not less than 30 minutes. (Col. 17:8-15) (A3585) (citing A75) (emphasis added)

The use of an oxidizing agent is clearly an option and but one example of how oxidation is done. Even though the District Court was aware that it "must tread carefully to avoid reading a limitation from the written description into the claims" (A3581), it did so with an optional example of oxidization that *may* be carried out.

The District Court also added to its claim construction that "all or substantially all" of the reduced CoQ_{10} must be converted to oxidized CoQ_{10}, without any explanation other than the construction proposed by Defendants. There is nothing in the specification or the file history that even implies that "all or substantially all" of the reduced CoQ_{10} obtained from the disruption step must be converted to oxidized CoQ_{10} as explained in greater detail below.

VI. SUMMARY OF THE ARGUMENT

A. Inert Gas Atmosphere

The District Court defined "inert gas atmosphere" as a "gas atmosphere that is free or substantially free of oxygen and reactive gases". (A 3578)

This claim term appears in independent claims 1 and 22, which are directed to a process for producing oxidized CoQ_{10}. The District Court however, specifically relied on a portion of the specification (Col. 16:35-48) directed to the production of reduced CoQ_{10} when defining this claim term. Reduced CoQ_{10} has to be protected from an oxidation reaction and therefore produced in a deoxygenized atmosphere as set forth at Col. 16, :35-48. Oxidized CoQ_{10} does not have to be protected from oxidation reaction but recovery of oxidized CoQ_{10} does have to be "carried out in consideration of general safe operation." (Col. 17:20-25). It was an error for the District Court to rely on the wrong portion of the specification when defining this claim term.

Safe operation is important during production of oxidized CoQ_{10} as an organic solvent is used during the extraction process and organic solvents are flammable. Safe operation requires the use of "a gas atmosphere that is less readily reactive with the organic solvent", the claim term definition proposed by Kaneka, but does not require a gas atmosphere that is deoxygenized, *i.e.*, free of oxygen.

Kaneka's definition is supported by the claim language. Independent claims 1 and 11 use the transitional term "comprises" which is an inclusive or open-ended transition term that does not exclude additional, unrecited elements. Dependent claim 9 specifically states that "inert gas atmosphere comprises nitrogen gas" meaning other gases may be present. Kaneka's definition allows for a percentage of oxygen, a reactive gas, to be included in an inert gas atmosphere as long as the "percentage of oxygen is limited to a threshold of safety below the point of combustion", a percentage agreed to by Defendant Shenzhou's expert, Dr. Bernard Trumpower, and Kaneka's expert, Dr. Jeffrey Kittendorf. (A7825-7827; A10218-10219)

B. Sealed Tank

The District Court defined "sealed tank" as a "tank that is closed to prevent the entry or exit of materials". In deciding on this definition, the District Court "adopt[ed] the reasoning presented in the ITC Proceeding . . . in its entirety". (A3579)

The ITC and the District Court relied entirely on extrinsic evidence for their respective claim constructions of this claim term. This approach was in error as the specification provides support for a correct definition.

Fig. 1 of the '340 patent illustrates a series of tanks used in Example 8 which is described at Col. 23:15-44 of the specification. Example 8 and Fig. 1

describe one embodiment of the invention and comprise the only description of tanks in the '340 patent. The tanks in Fig. 1 have various incoming and outgoing pipes or lines permitting the contents of the tanks to be exchanged. The tanks in Fig. 1 are certainly not "closed to prevent the entry or exit of materials" as advocated by the District Court.

A "sealed tank" is also required for safety considerations, as a flammable organic solvent should not be allowed to escape into the atmosphere. A "sealed tank" should also protect the contents of the tank from outside contamination. Therefore Kaneka's proposed definition for "sealed tank": "a tank that substantially prevents direct exposure of its contents to the atmosphere" takes into account the embodiment of Fig. 1 and the safety considerations set forth in the '340 patent.

C. Culturing Reduced Coenzyme Q10 Producing Microorganisms - - To Obtain Microbial Cells Containing Reduced Coenzyme Q10 At A Ratio Of Not Less Than 70 Mole % Among The Entire Coenzyme Q10

It is Kaneka's position that no claim construction is required for this claim term as the language is clear. The District Court however added two unsupported limitations to the claims:

i) The ratio of not less than 70 mole % must be reached at a time prior to the extraction, oxidation or disruption steps and

ii) The 70 mole % ratio must be measured as described at Col. 5:8-43, and Example 1 of the '340 patent.

There is nothing in the '340 patent or its file history that supports the first limitation. However, the District Court based the first limitation on the premise that the production steps of culturing, disruption, oxidizing and extraction must occur in order. This premise is wrong, as the '340 patent specifically allows oxidation for the production of oxidized CoQ_{10} to occur at any time during the production process, allows disruption and extraction to occur at the same time, and allows extraction to occur before or after oxidizing. Thus, the intrinsic evidence provides no support for the first limitation. In addition, the specification specifically says that culturing to obtain 70 mole % can be completed at the point when a desired amount of reduced coenzyme is produced, *i.e.*, at any time during the production process.

The District Court's second limitation is specifically based on one example from the specification, an example that applies to some of the claims but would exclude a multitude of other claims. This construction therefore violates the doctrine of claim differentiation, as well as impermissibly limiting all of the claims to one example in the specification.

Confidential Material Redacted

D. Oxidizing Thus-Obtained Reduced Coenzyme Q_{10} To Oxidized Coenzyme Q_{10} And Oxidizing The Extracted Reduced Coenzyme Q_{10} To Oxidized Coenzyme Q_{10}

Kaneka's position in the District Court was that no construction was required for this claim term. The District Court again added two unsupported limitations to the claims:

i) There must be "active" oxidation, meaning an oxidation agent must be used; and

ii) All or substantially all oxidation must occur in a separate step before or after the extraction step.

With respect to the first limitation, the District Court again incorporated one example of active oxidation into the claims in violation of the doctrine of claim differentiation. With respect to the second limitation, the District Court provided absolutely no support or reasoning, either intrinsic or extrinsic.

Both limitations are also in direct conflict with the specification, which allows the oxidation of oxidized CoQ_{10} to occur without protection from an oxidation reaction, [redacted]

VII. ARGUMENT

This court reviews a district court's claim construction *de novo*. *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1186 (Fed. Cir. 1998) (citing *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1148, 1456 (Fed. Cir. 1998) (en banc). Claim construction requires an examination of the claim language, the written description, and, if relevant, the prosecution history" and must begin with examination of the language of the claim. *Id.* There is a "heavy presumption" that a claim term should be given the ordinary meaning understood by a person of ordinary skill in the art ("POOSITA"). *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002) (citation omitted). Courts should interpret claims of patents according to the plain, accustomed meaning understood by a POOSITA at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313-14 (Fed. Cir. 2005)(en banc). "In some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words." *Id.* at 1314. Most of the

time a court is not required to define or re-write claim terms.[2] In the rare instances a court chooses to define claim terms, it should be done only to: (1) aid the jury in understanding a patent claim, without limiting its scope; or (2) address an express limitation admitted by a patentee to overcome prior art during prosecution of a patent.[3]

In claim construction, courts first examine the intrinsic evidence of the patent itself and the prosecution history to define the invention's scope. *See Phillips*, 415 F.3d at 1313-14.

"The court turns to extrinsic evidence only when the intrinsic evidence is insufficient to establish the clear meaning of the asserted claim." *Zodiac Pool Care, Inc. v. Hoffinger Ind., Inc.*, 206 F.3d 1408, 1414 (Fed. Cir. 2000).

[2] *Phillips*, 415 F.3d at 1312 ("Because the patentee is required to 'define precisely what his invention is,' . . . it is 'unjust to the public, as well as an evasion of the law, to construe it in a manner different from the plain import of its terms . . . [I]f we once begin to include elements not mentioned in the claim, in order to limit such claim … we should never know where to stop.") (citation omitted).

[3] *Omega Engineering, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1323 (Fed. Cir. 2003) ("We indulge a 'heavy presumption' that claim terms carry their full ordinary and customary meaning . . . unless the patentee unequivocally imparted a novel meaning to those terms or expressly relinquished claim scope during prosecution.") (citation omitted); *see also U.S. Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997) (holding a court should decline to construe claim terms that are not confusing to a jury); *Bd. Of Trustees of the Leland Stanford Univ. v. Roche Molecular Sys.*, 528 F.Supp.2d 967, 976 (N.D. Cal. 2007) (holding terms "do not need to be construed because they are neither unfamiliar to the jury, confusing to the jury, nor affected by the specification or prosecution history.") (citing *Phillips*).

Extrinsic evidence may be examined to determine how a term or phrase has been used and/or understood by a POOSITA. *Phillips*, 415 F.3d at 1318. Extrinsic evidence "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treaties." *Phillips* 415 F.3d at 1323 (quoting *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995)). Although extrinsic evidence can shed useful light on relevant art, it is considered less significant than the intrinsic record in determining the operative meaning of patent claim language. *Phillips*, 415 F.3d at 1317. "The Court may receive extrinsic evidence to educate itself about the invention and the relevant technology, but the court may not use extrinsic evidence to arrive at a claim construction that is clearly at odds with the construction mandated by the intrinsic evidence." *Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 971 (Fed. Cir. 1999).

A patent claim defines an invention. *Mere examples* in the *specification* ("embodiments") do *not*. "It is a 'bedrock principle' of patent law that 'the *claims* of a patent define the invention to which the patentee is entitled the right to exclude.'" *Phillips*, 415 F.3d at 1312 (quoting *Innova/Pure Water Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004)) (emphasis added). "Although the specification may aid the court in interpreting the meaning of disputed claim language, particular embodiments and examples

appearing in the specification will *not* generally be read into the claims." *Comark Communications, Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998) (quoting *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1571 (Fed. Cir. 1988)) (emphasis added); *see also Phillips*, 415 F.3d at 1323. It is imperative to avoid "one of the cardinal sins of patent law – reading a limitation from the written description into the claims." *Phillips*, 415 F.3d at 1320 (citing *Texas Digital Systems, Inc. v. Telegenix, Inc.*, 308 F.3d 1193 (Fed. Cir. 2002)). This Court has "expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment." *Phillips*, 415 F.3d at 1323.

The Defendants in this case disregarded the guiding principles of claim construction. Defendants' proposed constructions limited the asserted patent claims to mere examples of the invention in the written description of the patent. This Court has rejected this approach, sometimes attempted by accused infringers, by holding that mere examples in the specification cannot be used to limit the scope of a patent claim. *Phillips*, 415 F.3d at 1323.

Moreover, the Defendants in this case requested harsh limitation language, unsupported by the written description, to be added to the claims (such as "free or substantially free", "converting all or substantially all"). Their strategy was to shrink the patent's scope by adding new limitations, so that they

can argue they do not infringe. Such words, called by the Federal Circuit "words of manifest exclusion," are sometimes crafted by accused infringers to try to block infringement actions.[4] Defendants' proposed new words, when added to the '340 patent's claims, are so constrictive that they would even exclude the preferred embodiment.

Defendants were not trying to aid the jury's understandings of the patent claims. They wanted to limit the patent claims until they do not infringe. To do this, they try to limit the claims to one example in the written description, which is improper under Federal Circuit case law. They also inserted words of manifest exclusion which exclude the preferred embodiment. Such a "construction is . . . rarely, if ever, correct."[5] "We normally do not interpret claim terms in a way that excludes embodiments disclosed in the specification."[6] By alternately limiting the claims to one example and/or excluding the preferred embodiment, the Defendants lead the District Court into error.

[4] *See Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 905 (Fed. Cir. 2004). These cannot be imported into the plain language of the claim unless the defendant is able to point to a specific example of the patentee's clear intent to have such words included – an almost impossible standard to meet. *Id*.

[5] *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996).

[6] *Oatey Co. v. IPS Corp.*, 514 F.3d 1271, 1276-77 (Fed. Cir. 2008) (citing *Verizon Servs. Corp. v. Vonage Holdings Corp.*, 503 F.3d 1295, 1305 (Fed. Cir. 2007) (rejecting proposed claim interpretation that would exclude disclosed examples in the specification).

Kaneka asserts that a POOSITA to which the subject matter of the '340 patent pertains should, minimally, have a degree in microbiology, biochemistry, or chemical engineering, with particular experience in the field of bioprocesses – which involves using living cells or enzymes to produce a product. This level of experience required for a skilled artisan will vary with the level of the individual's education. Under *Markman*, Kaneka asserts that the claims should be understood from the perspective of such a POOSITA.

A. "Inert Gas Atmosphere"

Kaneka's Construction	District Court's Construction
A gas atmosphere that is less readily reactive with the organic solvent	A gas atmosphere that is free or substantially free of oxygen and reactive gases.

The District Court's claim construction of "inert gas atmosphere" was based primarily on the specific language in Col. 16:35-48 of the specification. It is necessary, however, to put that language in context by referring to earlier language in Col. 16 as set forth below:

> In recovering *reduced* coenzyme Q10, it is preferable to be careful so that reduced coenzyme Q_{10} is not decomposed (e.g. so that reduced coenzyme Q_{10} is not oxidized to oxidized coenzyme Q_{10}). (Col. 16:15-18) (A74) (*emphasis added*)

The next paragraph refers to the previous paragraph cited above and states:

> By the above-mentioned conditions, an oxidation reaction can be substantially prevented and, optionally, more strictly the above-mentioned cell disruption and/or extraction are preferably carried out under the condition that *reduced* coenzyme Q_{10} is protected from an oxidation reaction. It is preferable to carry out at least the extraction under this condition and it is more preferable to carry out the disruption and the extraction under this condition. (Col. 16:27-34) (A74) (*emphasis added*)

The next paragraph is the language relied on by the District Court which states:

> As the condition that reduced coenzyme Q10 is protected from an oxidation reaction means, for example, a deoxygenized atmosphere (an atmosphere of an inert gas such as nitrogen gas, carbon dioxide gas, helium gas, argon gas or hydrogen gas, reduced pressure, a boiling condition); a high salt concentration condition. (Col. 16:35-48) (A74) (*emphasis added*)

The cited paragraphs, when taken in context, cannot be clearer that this section of the specification is referring to the extraction and recovery of *reduced* CoQ_{10}. As mentioned above, the '340 patent is based on a divisional application from the parent application that contained claims directed to the recovery of both reduced and oxidized CoQ_{10} and in which the specification covered the process to produce both types of CoQ_{10}.

However, the '340 patent claims are directed only to the production of oxidized CoQ_{10}. Oxidized CoQ_{10} does not have to be protected from an oxidation reaction as specifically stated in the portions of the specification describing the production of oxidized CoQ_{10} at Col. 17:20-25:

> Incidentally, it is not necessary to carry out the recovery of oxidized coenzyme Q_{10} under 'the condition that reduced coenzyme Q_{10} is protected from an oxidation reaction', which is recommended for the recovery of reduced coenzyme Q_{10} and the recovery may be carried out in consideration of general safe operation and the like. (A75)

It was error for the District Court to rely on a section of the patent specification, specifically limited to the recovery and extraction of reduced CoQ_{10}, to interpret a claim term in a claim describing the recovery and extraction of oxidized CoQ_{10}.

The language cited immediately above also calls for recovery to be carried out in consideration of "general safe operation." Safe operation is important because an organic solvent is used during extraction and organic solvents are flammable.

[redacted]

[redacted]Hexane is a Class 1B flammable liquid and precautions must be taken to avoid its combustion. (A7933) Due to the organic solvents combustion potential, the '340 patent describes the extraction of oxidized CoQ_{10} "in consideration of general safe operation and the like" including extraction in an "inert gas atmosphere" and/or a "sealed tank" while recognizing that complete oxygen elimination is very difficult to achieve when operating at an industrial scale. (Col. 10:60-61) (A71)

It is Kaneka's position that an "inert gas atmosphere" is not a deoxygenized atmosphere, as advocated by the Defendants and the District Court, as a "deoxygenized atmosphere" is only necessary when producing reduced $CoQ_{10.}$ However, there must be no more than a limited amount of oxygen present during extraction to prevent fire or explosion in accordance with the general safe operation of the production process. The amount of oxygen that can be present during the extraction step and still guarantee safe operation is shown scientifically to be less than 12%. (Declaration of Kaneka Expert Dr. Jeffrey Kittendorf) (A7825-7827) Kaneka's reasoning is also supported by Dr. Bernard L. Trumpower, who was Defendant Shenzhou's expert during the ITC Litigation. Dr. Trumpower, a POOSITA, stated the following in his ITC Rebuttal Report:

> Another reason to extract coenzyme Q_{10} under an inert gas atmosphere is to protect against fire or explosion. Organic solvents such as heptane, hexane, petroleum ether, isooctane, and benzene are volatile and flammable. Since sparks from machines or other sources of a flame could ignite these volatile organic solvents in the presence of oxygen, extraction of coenzyme Q_{10} is frequently performed under an inert gas atmosphere in order to exclude oxygen. (A9768)
>
> * * *
>
> In my opinion, a person of ordinary skill in the art would also know that an inert gas atmosphere is used during extraction of both oxidized and reduced coenzyme Q_{10} to decrease the potential for oxygen to ignite the organic solvent, such as hexane, and cause an explosion. Displacing "some oxygen" in the atmosphere with an inert gas would not prevent the organic solvent from igniting.

> Instead, the percentage of oxygen would have to be limited to a threshold of safety below the point of combustion. (A10218-10219)

Kaneka agrees with Dr. Trumpower's analysis and that is why Kaneka proposed that "inert gas atmosphere" should mean "a gas atmosphere that is less readily reactive with the organic solvent." Judge Gilmore's claim construction in the Texas Litigation is another acceptable definition of "inert gas atmosphere", defined as "a gas atmosphere that is substantially free of reactive gases." (A3337) Both definitions are in accordance with the teachings in the '340 patent and take rationally into account the safety considerations inherent when using organic solvents.

Further support to demonstrate that the inventors did not intend to limit "inert gas atmosphere" to an atmosphere completely without oxygen is shown by the claim language.

The use of the phrase "comprises" in the claims signals that the claims are open, not closed: "the transitional term 'comprising,' which is synonymous with 'including,' 'containing,' or 'characterized by,' is inclusive or open-ended and does not exclude additional, un-recited elements or method steps."[7] Because the claims at issue here use the transitional term "comprises," the claims are

[7] *See Manual of Patent Examining Procedure*, §2111.03 (rev. July 2010) (citing *Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368 (Fed. Cir. 2003) ("The transition 'comprising' in a method claim indicates that the claim is open-ended and allows for additional steps.").

presumed to be open-ended, which allows for the inclusion of unspecified elements such as oxygen. If Kaneka had intended that the extraction step occur in an atmosphere with no oxygen whatsoever, the patentee could have claimed such an atmosphere by using the transitional phrase "consisting of." Kaneka chose not to do so, and instead recited the term "comprising" in conjunction with "inert gas atmosphere." The patentee's intent must be given its effect. Similarly, dependent claims 9, 20, and 30 state that the "inert gas atmosphere comprises nitrogen gas". (Col. 24:46-47, Col. 25:24-25, Col. 26:5-6) Because the claims state that the "inert gas atmosphere comprises nitrogen gas," it could contain other gases that may or may not be inert gases such as nitrogen.

The specification supports this open-ended construction. In an industrial production of oxidized CoQ_{10}, protection from oxidation during extraction is unnecessary as long as the process is carried out "in consideration of general safe operation and the like". (Col. 17:20-25) (A75)

In light of the specification, a POOSITA would understand that when producing oxidized CoQ_{10}, the "inert gas atmosphere" claim language does not require an atmosphere free or substantially free of oxygen. All that is suggested by the specification with regard to oxidation of reduced CoQ_{10} is that the extraction should be carried out in a safe manner, *i.e.*, under a gas atmosphere that is less readily reactive with the organic solvent and more conducive to safe

operation. Accordingly, this claim term should be construed to mean "extracting . . . under a gas atmosphere that is less readily reactive with the organic solvent," or construed to mean the definition adopted by Judge Gilmore in the Texas Litigation who specifically took into account safety considerations when defining "inert gas atmosphere" as "a gas atmosphere that is substantially free of reactive gases."

B. "Sealed Tank"

Kaneka's Construction	**District Court's Construction**
A tank that substantially prevents direct exposure of its contents to the atmosphere.	A tank that is closed to prevent the entry or exit of materials.

The District Court adopted "in its entirety" the definition of "sealed tank" adopted by the ALJ in the ITC Litigation. Therefore, we must consider the reasoning of the ALJ. (A3579)

The ALJ relied on extrinsic evidence and pointed to the dictionary meaning of "seal".[8] (A5347) Based on this extrinsic evidence the ALJ concluded that "sealed tank" meant "a tank that is closed to prevent the entry or exit of materials". (A5351)

[8] The ALJ also pointed to the testimony of Kaneka's expert, Dr. Connors, who agreed that the dictionary definition of "sealed" meant "airtight." (A5347) However, there is nothing in Dr. Connors' ITC testimony where he agreed that "sealed tank" meant "air tight" and of course Dr. Connors would have no choice but to agree to a dictionary definition of "sealed".

Judge Gilmore, in the Texas Litigation rejected reliance on only extrinsic evidence and turned to the '340 patent to reach a decision on the proper definition for "sealed tank." Her reasoning is the following:

> The Court first considers Kaneka's proposed construction of "extracting . . . in a sealed tank" as "extracting … in a tank that substantially prevents direct exposure of its contents to the atmosphere". This construction allows the entry and exit of substances from the tank during extraction as long as the tank's contents are not exposed to the atmosphere. Kaneka's emphasis on preventing exposure to the atmosphere is consistent with the patent specification's discussion of safety concerns, although, as ZMC points out, the patent specification does not specifically link sealed tanks to safety concerns. In addition, Kaneka's position that a "sealed tank" may nonetheless allow for substances to enter and exit is one which is consistent with the tanks depicted in Figure 1, because those tanks allow for substances to flow between each other. Although Figure 1 is not captioned or described as depicting sealed tanks, it is also not captioned or described in a such a way that prevents it from being interpreted as a depiction of sealed tanks. Because it is the only picture of tanks contained in the patent, it supports Kaneka's portion that sealed tanks would allow for the entry and exit of substances. Furthermore, as Kaneka has argued, the patent claims processes which are for industrial scale production. In that context, it makes sense for sealed tanks to have certain vents or valves to release evaporation from the production processes.
>
> In contrast to Kaneka's proposed construction, ZMC's proposed construction relies solely on extrinsic evidence, from other definitions of sealed tanks, and from inventor testimony. The Court therefore declines to adopt ZMC's proposed construction. However, the Court also declines to adopt the entirety of Kaneka's proposed construction. Kaneka has failed to explain why the words "substantially" and "direct" should be included in its proposed construction. For example, Kaneka has not explained how "substantially" preventing exposure differs from preventing exposure, of how "direct exposure" differs from "exposure". The

> Court therefore declines to use "substantially" and "direct" in its construction. Accordingly, the court finds that "extracting the oxidized coenzyme Q_{10} by an organic solvent in a sealed tank" means "**extracting the oxidized coenzyme Q_{10} by an organic solvent in a tank that prevents exposure of its contents to the atmosphere".** (A3341-3342)

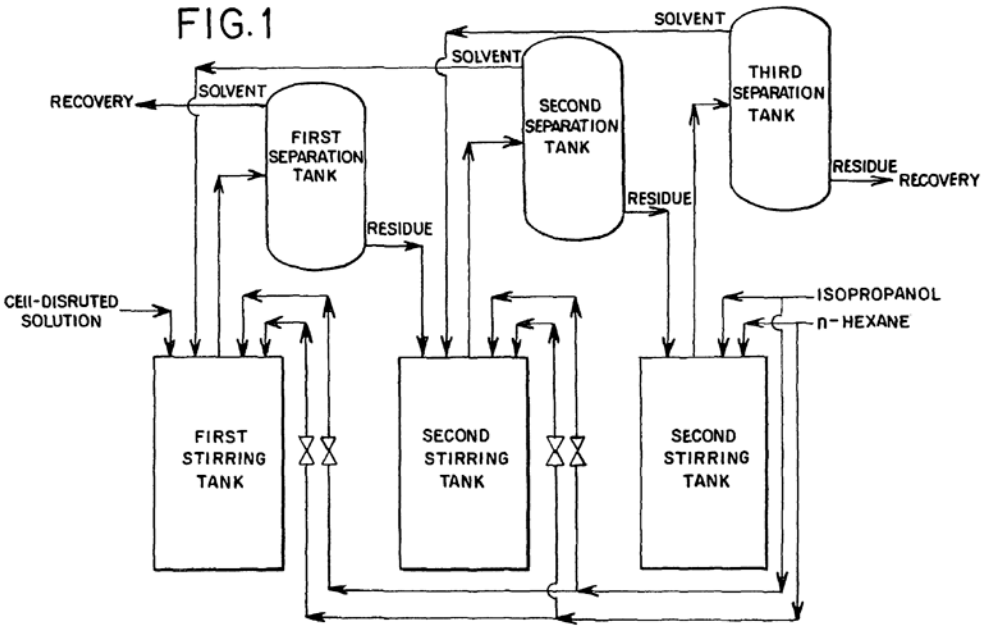
A sealed tank is related to safety considerations because a flammable organic solvent, such as hexane is used in the extraction tank. This raises two safety concerns: (1) the flammable organic solvent should not be allowed to escape to the atmosphere for environmental and safety reasons and (2) a flammable organic solvent such as hexane, vaporizes and creates hexane gas vapors. The hexane vapors substantially increase the pressure inside the extraction tank which, therefore, requires a release valve to make sure the pressure does not rupture the tank. (A5349-5351) For industrial applications, when hexane gas is released via a release valve, the hexane is directed to a condenser which converts the hexane gas back to liquid hexane which is returned to the production process. (A7939-7942)

Therefore, Kaneka's construction of "extracting . . . in a sealed tank" correctly reflects the understanding of one skilled in the art in light of the claims and the intrinsic evidence. The specification expressly states that "it is not necessary to carry out the recovery of oxidized coenzyme Q_{10} under 'the condition that reduced coenzyme Q_{10} is protected from an oxidation reaction,'"

but that instead "the recovery may be carried out in consideration of general safe operation and the like."

The "sealed tank" limitation was added at the same time as the "industrial scale" limitation. (A3126-3144) Given the above evidence, a POOSITA would understand that "sealed tank" should be interpreted in light of general safe operations in an industrial scale production – *i.e.*, a tank that prevents direct exposure of its contents to the atmosphere and, thus minimizes exposure of potentially hazardous material to the atmosphere. The specification plainly supports this construction.

Figure 1 and Example 8 of the '340 patent describe an embodiment in which countercurrent 3-step continuous extraction is employed using a series of "sealed tanks." While these tanks are "sealed tanks," the tanks have various incoming and outgoing pipes or lines permitting the contents of the tanks to be exchanged as shown in Fig. 1 below:



The specification itself is more than sufficient to reasonably apprise one of ordinary skill in the art as to the meaning of "sealed tank." A "sealed tank" is a tank whose contents are not directly exposed to the outside atmosphere, but is not absolutely closed off from other tanks.

Defendants proposed an overly narrow construction that is inconsistent with the claims and the specification, a construction that was adopted by the District Court in error. The District Court's construction requires that "sealed tank" be "a tank that is closed to prevent the entry or exit of materials." This construction directly contradicts the disclosure in Figure 1 and Example 8 of the specification. Figure 1 depicts the flow of materials from one "sealed tank" to another. Thus, a construction of "sealed tank" cannot require that a tank be completely shut off from other tanks. The District Court's construction would

prevent the exchange of materials between tanks during extraction, which is a key part of one embodiment.

Further, claims 27-28 and 39-40 require that extraction not only occur in a "sealed tank" but also include "continuous extraction" and/or "countercurrent multistage extraction." Materials must be able to flow in and out of the extraction tanks during extraction. The District Court's construction is inconsistent with the claims themselves.

Kaneka's construction of "sealed tank" as "a tank that substantially prevents direct exposure of its contents to the atmosphere" reflects a reasonable understanding of how one of ordinary skill in the art would understand this claim term in light of the intrinsic evidence.

C. "Culturing Reduced Coenzyme Q10 Producing Microorganisms … To Obtain Microbial Cells Containing Reduced Coenzyme Q_{10} At A Ratio Of Not Less Than 70 Mole % Among The Entire Coenzyme Q_{10}"

Kaneka's Construction	District Court's Construction
No construction necessary.	Culturing reduced coenzyme Q_{10} producing microorganisms to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10} at a time prior to the extracting, oxidation or disruption steps and as determined by the assay described at Col. 5, l. 8 to l. 43, and Example 1 of the '340 patent.

This claim term was not disputed in the Texas Litigation and the precise term construed in the District Court was not construed by the ALJ in the ITC Litigation. Kaneka shall first address the District Court's construction that the mole % of reduced CoQ_{10} must be determined at a time prior to the extraction, oxidation or disruption steps. The District Court reached this conclusion based on the premise that the steps of the process, *i.e.*, culturing, disruption, oxidizing and extraction must be performed in the order listed. (A3581-3582)

It is clear from the claims that oxidation and extraction can occur in any order as claim 1 calls for oxidation before extraction and claim 11 calls for extraction before oxidizing. In addition, at Col. 9:19-21 in the specification, it

states; "It is needless to say that the cell disruption and extraction can be carried out at the same time". Also the specification states at Col. 17:20-23 that; "Incidentally, it is not necessary to carry out the recovery of oxidized coenzyme Q_{10} under the condition that reduced coenzyme Q_{10} protected from an oxidation reaction –". This makes it clear that since protection from an oxidation reaction is not necessary, oxidation can and will happen throughout the production process, and therefore does not appear in any particular order.

The District Court also specifically referred to "modifiers" in the claim language like "thus-obtained" and "the extracted reduced" in support of its position. (A3581) However, the claim "modifiers" do not compel the conclusion that the production steps must be performed in the order listed. For example, claims 1 and 22 in the '340 patent include the phrase "oxidizing the *thus-obtained* reduced coenzyme Q_{10} to oxidized coenzyme Q_{10} . . . . ."

As set forth above, reduced CoQ_{10} continues to increase in the culturing step as long as the microorganisms have a sufficient food source, and oxidation is also continually occurring in the culturing step. Therefore, from the commencement of the culturing step "thus obtained" reduced Co Q_{10} is being oxidized long before the ratio of 70 mole % is reached and long before there is any disruption or extraction.

The same analysis applies to "the extracted reduced" modifier in claims 11 and 33 which reads "oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}." Since oxidizing occurs throughout the process, including during the extraction process and reduced CoQ_{10} can be produced as long as the microorganisms have a food source, the entire phase "oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" can occur during extraction.

By looking only at the claim language, and not including a review of specific language in the specification, the District Court erred by deciding all steps in the production method must be performed in a specific order. Oxidation occurs throughout the process and disruption and extraction can occur at the same time. Therefore the specification specifically teaches that the steps of the process do not have to occur in the order listed.

It is submitted that the District Court's premise, to arrive at the conclusion that there is a specific time for sampling for 70 mole %, is fundamentally flawed as the specification teaches that the production steps can occur in any order and nothing in the specification or the file history discusses or refers to a specific time to achieve 70 mole %.

It is a fact that the amount of reduced CoQ_{10} can potentially continue to increase as long as culturing continues, and culturing continues as long as the

food supply lasts for the microorganisms. Therefore, there is no specific point when 70 mole % must be reached as specifically stated in the specification;

> The culture can be completed at the point when a desired amount of reduced coenzyme is produced. (Col. 8:54-55) (A70)

The District Court's construction also limits the claims to a mere example from the specification (Example 1 and the testing method described in Col. 5:8-43). "Although the specification may aid the Court in interpreting the meaning of disputed claim language, particular embodiments and examples appearing in the specification will not generally be read into the claims." *Comark Communications, Inc.*, 156 F.2d at 1187 (quoting *Constant v. Advanced Micro-Devices, Inc*., 848 F.2d 1560, 1571 (Fed. Cir. 1988)); *see also Phillips*, 415 F.3d at 1323. It is imperative to avoid "one of the cardinal sins of patent law – reading a limitation from the written description into the claims". *Phillips*, 415 F.3d at 1320 (quoting *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1343-44 (Fed. Cir. 2001)).

Although the preferred embodiment describes one method to measure the mole % ratio, the claims define the invention as a process for producing CoQ_{10} – not a process for measuring CoQ_{10}. No requirement for a specific measuring or testing method can be found anywhere in the language of the claims. The claim construction adopted by the District Court is, again, impermissibly attempting to

limit the '340 patent's claims to be the preferred embodiment *See e.g., TI Group Auto Sys (N. Am.), Inc. v. VDO N. Am., LLC*., 375 F.3d 1126, 1138.

Example 1 (Col. 17:43 - Col. 20:33) is merely one of eight examples of producing CoQ_{10} provided by the specification. If the "70 mole %" language was limited only to Example 1, this would exclude the other seven examples of the patented process. The claim construction adopted by the District Court ignores the fact that the specification states:

> [t]he above mentioned content of the reduced coenzyme Q_{10} and ratio of reduced coenzyme Q_{10} among the entire coenzymes Q_{10} **can be** confirmed by physically disrupting the microbial cells … (Col. 5:8-11) (emphasis added)

The District Court's construction would limit <u>all</u> of the claims to the method described in Example I. The Federal Circuit in *Netcraft Corp. v. Ebay Inc. et al.*, 549 F.3d 1394, 1400 (Fed. Cir. 2008) held that the specification's use of an example that "<u>can be</u>" utilized does not limit the claimed invention:

> In addition, *Netcraft* attributes significance to the omission of financial services companies from the following portion of the specification:
>
> Such providers **can be**, for **example**, companies whose only business is to offer connection to the Internet, companies which offer on-line computer services, one of which is connection to the Internet, cable television companies, or telephone companies." '739 **Patent** Col. 12, :61-65. As the District Court determined, however, "[a]lthough the patent does not include financial service companies in its list of ***examples*** of internet access providers, *e.g.*, '739 patent, Col. 2, :61-65, that does not mean that such companies

> *cannot* be providers. An invention is not limited to its examples.

In addition, the claim construction adopted by the District Court would limit the "70 mole %" language, a limitation found in every claim, to a process that requires extraction by "physically disrupting the microbial cells." This construction would exclude claims 11-13, 15-21, 33-35, and 37-45, which do not require "disrupting the microbial cells." Only claims 1-10, 14, 22-32, and 34 require "disrupting the microbial cells." This construction violates the doctrine of claim differentiation. *Vitronics Corp.*, 90 F.3d at 1582. If all of the claims were limited to "disrupting the microbial cells", what could be the purpose of including this limitation in some of the claims but not in others?

Moreover, the specification provides specific alternatives to "physically disrupting the microbial cells" including "chemical treatment, an enzymic treatment as well as a heating treatment, an autolysis, an osmolysis, a plasmoptysis and the like." (Col. 9:33-38) If the "70 mole %" language is limited to "physically disrupting," then the claims would exclude the numerous non-physical disrupting methods disclosed in the specification. The Federal Circuit has held that "rarely, if ever" does a patentee draft claims which exclude his or her own examples of the invention, and cautioned against interpreting terms "in a way that excludes embodiments disclosed in the specification".

Oatey Co. 514 F.3d at 1276-1277. It was error for the District Court to adopt a claim construction that excludes the inventors' own examples.

D. "Oxidizing *Thus-Obtained* Reduced Coenzyme Q_{10} to Oxidized Coenzyme Q_{10}" And "Oxidizing *The Extracted* Reduced Coenzyme Q_{10} To Oxidized Coenzyme Q_{10}"

Kaneka's Construction	**District Court's Construction**
No construction necessary, (i.e., "oxidizing thus obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" and" oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}".	Actively converting all or substantially all of the reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a step before beginning the extraction step, and Actively converting all or substantially all of the extracted reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a separate step after the extraction step has been performed.

For this claim term, not construed in either the Texas or ITC Litigations, the District Court adopted, in its entirety, the Defendants' proposed construction. (A3584-3586) Kaneka has two fundamental objections to this claim construction; (1) that the reduced CoQ_{10} must be actively converted to oxidized CoQ_{10} and (2) that all or substantially all of the reduced CoQ_{10} must be converted to oxidized CoQ_{10} in a single step. Each objection is considered below.

The District Court based its added limitation of active oxidization on "examples of the oxidizing step using an oxidizing agent". (A3585) Those "examples" are described at Col. 17:8-42 and Col. 20:60-Col. 21:42. This Court has consistently cautioned against relying on such exemplars to limit the claims:

> Confirming the claim in light of the specification does not however, imply that limitations discussed in the specification may be read into the claims. It is therefore, important not to confuse exemplars or preferred embodiments in the specification that serve to teach and enable the invention with limitations that define the outer boundaries of claim scope. *Intervet Inc. v. Merial Ltd.*, 617 F.3d 1282, 1287 (Fed. Cir. 2010) (citing *Phillips* at 1312-13).

It is respectfully submitted that the District Court erred by limiting all of the independent claims with an exemplary disclosure in the specification when nothing else in the claim or the specification imply that active oxidization is a required part of the invention described in the independent claims. Indeed, the use of an oxidizing agent is specifically claimed in dependent claims 4, 15, 25 and 37 so that adding "active" oxidation to the independent claims is a violation of the doctrine of claim differentiation. *See Phillips*, 415 F. 3d at 314 (holding that when a dependent claim limits an independent claim it is presumed that the independent claim does not include that limitation).

In the District Court Defendant's argued that the independent claims must be limited to "active oxidation" based primarily upon Kaneka's in-house attorney's notes, in Japanese, regarding an interview with the PTO Examiner. In

the notes, not part of the intrinsic record, Kaneka's in-house attorney allegedly distinguished a prior art reference on the basis of "active oxidation". (A 03428) Even assuming that the personal notes of Kaneka's attorney could be considered evidence, the PTO Examiner specifically rejected any attempt to distinguish the claimed invention on the basis of "active oxidation." (A 03477-03478)

There is also no basis for the District Court's decision that "all or substantially all of the reduced CoQ_{10} must be oxidized in a single step", except for it being the Defendants proposed claim construction. In Defendants' Responsive Claim Construction Brief Defendants argue that if the sets of claims in the '340 patent are to be differentiated then the language of claims 1 and 22 **must imply** oxidizing all or substantially all of the coenzyme Q_{10} before the extraction step. "Otherwise it is rather meaningless to speak of the relative **order** of oxidizing and extracting steps." (A3532) (emphasis added)

As explained above there is no fixed "order" to the production steps and any alleged order certainly does not "imply" that "all or substantially all" of the reduced CoQ_{10} must occur in a single step. There is absolutely no support, anywhere in the '340 patent or the prosecution history, that would require "all or substantially all" of the oxidation to occur in a single step. In fact, the specification at Col. 17:20-25 says the opposite, as the recovery of oxidized CoQ_{10} does not have to be protected from an oxidation reaction, oxidation can

and does occur throughout the production process. Judge Gilmore, in the Texas claim construction, specifically rejected adding this unsupported limitation to the claim language stating that " . . .the fact that oxidized CoQ_{10} is an end product does not mean that 'all or substantially all' of the extracted CoQ_{10} must be oxidized." (A 3351) The Defendants however define "substantially all" as requiring that "99.99%" of the coenzyme Q_{10} be oxidized prior to extraction. (A 3532) This Court should not import this groundless limitation into the claims.

Kaneka proposed that no construction was necessary for this claim term as the plain meaning of the words would be clear to a person of ordinary skill and to a jury. Defendant's proposed construction has absolutely no support, either extrinsic or intrinsic, and was proposed only to avoid infringement. The District Court adopted Defendants proposed definition in error and without analysis. Therefore, Kaneka submits that no construction is required for this claim term.

VIII. CONCLUSION

The District Court erred in construing all four claim terms discussed above. Kaneka respectfully requests this Court to vacate the District Court's Claim Construction Order and to remand this case to the District Court for further proceedings consistent with the correct construction.

Respectfully submitted,

/s/ Keith D. Nowak
Keith D. Nowak
Carter Ledyard & Milburn LLP
2 Wall Street
New York, NY 10005
(212) 732-3200
nowak@clm.com

Robert M. Bowick, Jr.
Raley & Bowick, LLP
1800 Augusta Drive, Suite 300
Houston, Texas 77057
(713) 429-8050
rbowick@raleybowick.com

Counsel for Plaintiff-Appellant
Kaneka Corporation

ADDENDUM

ADDENDUM TABLE OF CONTENTS

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA
WESTERN DIVISION

KANEKA CORPORATION,
Plaintiff,
v.
ZHEJIANG MEDICINE CO., LTD., ZMC-USA, L.L.C., XIAMEN KINGDOMWAY GROUP COMPANY, PACIFIC RAINBOW INTERNATIONAL INC., MITSUBISHI GAS CHEMICAL COMPANY, INC., MAYPRO INDUSTRIES, INC., and SHENZHOU BIOLOGY & TECHNOLOGY CO., LTD.,
Defendants.

Case No. 2:11-CV-2389-MRP (SSx)

JUDGMENT

The Court, having (1) granted-in-part Defendants Xiamen Kingdomway Group Company ("XKGC") and Pacific Rainbow International Inc.'s ("PRI") Motion for Summary Judgment of Noninfringement of U.S. Patent No. 7,910,340 ("'340 Patent") on December 6, 2013 (Dkt. No. 310); (2) granted-in-part Defendant Shenzhou Biology & Technology Co., Ltd.'s ("Shenzhou") Motion for Summary Judgment of Noninfringement of the '340 Patent on December 6, 2013 (Dkt. No. 311); (3) denied Plaintiff Kaneka Corporation's ("Kaneka") Motion for Summary Judgment of Validity of the '340 Patent as moot and dismissed the counterclaims of Shenzhou, XKGC, and PRI (hereinafter collectively referred to as "Defendants") for a Declaratory Judgment of Invalidity of the '340 Patent and a Declaratory Judgment of Unenforceability of the '340 Patent as moot on February 24, 2014 (Dkt. No. 313); and (4) granted Kaneka's Motion for Summary Judgment Dismissing XKGC's Counterclaims Three Through Nine on February 25, 2014 (Dkt. No. 314),

IT IS HEREBY ORDERED, ADJUDGED, AND DECREED that:

1. Kaneka's Amended Complaint, and each and every claim alleged therein, is dismissed with prejudice as to Shenzhou, XKGC, and PRI;

2. Defendants' counterclaims for Declaratory Judgment of Invalidity and Unenforceability of the '340 Patent are dismissed without prejudice as moot;

3 Judgment is entered in favor of Shenzhou, XKGC, and PRI, and against Kaneka, as to the Amended Complaint;

4. Kaneka shall recover nothing in this action as to Shenzhou, XKGC, and PRI; and

5. Shenzhou, XKGC, and PRI shall be entitled to recover their costs pursuant to the procedures set forth in Local Rule 54-1 through 54-9.

IT IS SO ORDERED.

DATED: March 27, 2014

Mariana R. Pfaelzer

Hon. Mariana R. Pfaelzer
United States District Judge

(12) **United States Patent**
Yajima et al.

(10) **Patent No.: US 7,910,340 B2**
(45) **Date of Patent: Mar. 22, 2011**

(54) **PROCESSES FOR PRODUCING COENZYME Q10**

(75) Inventors: **Kazuyoshi Yajima**, Hyogo (JP); **Takahisa Kato**, Hyogo (JP); **Akihisa Kanda**, Osaka (JP); **Shiro Kitamura**, Hyogo (JP); **Yasuyoshi Ueda**, Hyogo (JP)

(73) Assignee: **Kaneka Corporation**, Osaka-shi (JP)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 588 days.

(21) Appl. No.: **11/981,181**

(22) Filed: **Oct. 31, 2007**

(65) **Prior Publication Data**

US 2008/0171373 A1 Jul. 17, 2008

Related U.S. Application Data

(62) Division of application No. 10/500,249, filed as application No. PCT/JP02/13766 on Dec. 27, 2002, now abandoned.

(30) **Foreign Application Priority Data**

Dec. 27, 2001 (JP) 2001-398545

(51) **Int. Cl.**
C12P 1/00 (2006.01)
C12P 7/66 (2006.01)

(52) **U.S. Cl.** **435/133**; 435/41

(58) **Field of Classification Search** ..... None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,769,170	A *	10/1973	Kondo et al.	435/133
4,220,719	A	9/1980	Aida et al.	
6,156,802	A	12/2000	Mae et al.	

FOREIGN PATENT DOCUMENTS

DE	236 552	A1	11/1986
EP	0 051 921	A1	5/1982
EP	0 073 134	A2	3/1983
EP	0 956 854	A1	11/1999
EP	1 123 979	A1	8/2001
EP	1 336 657	A1	8/2003
EP	1 354 957	A1	10/2003
EP	1 386 905	A1	2/2004
EP	1 391 515	A1	2/2004
EP	1 408 024	A1	4/2004
EP	1 415 969	A1	5/2004
EP	1 415 970	A1	5/2004
EP	1 415 971	A1	5/2004
EP	1 415 972	A1	5/2004
EP	1 415 973	A1	5/2004
EP	1 440 962	A1	7/2004
EP	1 452 174	A1	9/2004
GB	930752		7/1963
JP	48-8836	B	3/1973
JP	54-110388	A	8/1979
JP	54-119090	A	9/1979
JP	55-27	A	1/1980
JP	55-28	A	1/1980
JP	55-21756	A	2/1980
JP	55-68295	A	5/1980
JP	55-148084	A	11/1980
JP	56-55196	A	5/1981
JP	56-154994	A	11/1981
JP	56-154996	A	11/1981
JP	57-33599	A	2/1982
JP	57-70834	A	5/1982
JP	60-75294	*	4/1985
JP	60-75294	A	4/1985
JP	10-57072	A	3/1998
JP	10-109933	A	4/1998
JP	10-330251	A	12/1998
JP	2001-61478		3/2001
WO	WO 96/17626		6/1996

OTHER PUBLICATIONS

Takada et al. Biochimica et Biophysica Acta. 1982, 679:308-314.*

Yoshida et al. "Production of ubiquinone-10 using bacteria". Journal of General and Applied Microbiology. 1998, 44:19-26.*

Disch, Andrea et al., "On the Absence of the Glyceraldehyde 3-Phosphate/Pyruvate Pathway for Isoprenoid Biosynthesis in Fungi and Yeasts," FEMS Microbiology Letters, vol. 168, No. 2, 1998, pp. 201-208.

Kockova-Kratochvilova, A. et al., "Die Beziehungen innerhalb der Gattung *Cryptococcus* (Sanfelice) Vuillemin", *Zbl. Bakt. Abt. II, Bd.*, vol. 131, No. 7, 1976, pp. 610-631.

Natori, Y. et al., "Production of Coenzyme Q_{10} by *Pseudomonas* N842", *Agric. Biol. Chem.*, vol. 42, No. 9, 1978, pp. 1799-1800.

Natori, Y. et al., "Enhancement of Coenzyme Q_{10} Accumulation by Mutation and Effects of Medium Components on the Formation of Coenzyme Q Homologs by *Pseudomonas* N842 and Mutants", *Agric. Biol. Chem.*, vol. 45, No. 10, 1981, pp. 2175-2182.

Ohta, H. et al., "*Agromonas oligotrophica* gen. nov., sp. nov., a Nitrogen-Fixing Oligotrophic Bacterium", Antonie van Leeuwenhoek, vol. 49, Nos. 4-5, 1983, pp. 429-446.

Sakato, K. et al., "Agitation-Aeration Studies on Coenzyme Q_{10} Production Using *Rhodopseudomonas spheroides," Biotechnology and Applied Biochemistry*, vol. 16, No. 1, 1992, pp. 19-28.

(Continued)

Primary Examiner — Vera Afremova
(74) *Attorney, Agent, or Firm* — Westerman, Hattori, Daniels & Adrian, LLP

(57) **ABSTRACT**

The present invention relates to a process for producing reduced coenzyme Q_{10} which comprises obtaining microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10}, optionally disrupting the cells and recovering thus-produced reduced coenzyme Q_{10}. The present invention also relates to a process for producing oxidized coenzyme Q_{10} which comprises either recovering oxidized coenzyme Q_{10} after oxidizing the above-mentioned microbial cells or disrupted product thereof, or recovering reduced coenzyme Q_{10} from the above-mentioned microbial cells or disrupted product thereof to oxidize thus-obtained reduced coenzyme Q_{10} thereafter. According to the processes of the present invention, reduced coenzyme Q_{10} and oxidized coenzyme Q_{10} can be produced simply on the industrial scale.

45 Claims, 1 Drawing Sheet

OTHER PUBLICATIONS

Urakami T., et al., "Production of Isoprenoid Compounds in the Facultative Methylotroph *Protomonas extroquens", J. Ferment. Technol*., vol. 66, No. 3, 1988, pp. 323-332.

Urakami, T. et al., "Production of Ubiquinone and Bacteriochlorophyll α by *Rhodobacter sphaeroides* and *Rhodobacter sulfidophilus", Journal of Fermentation and Bioengineering*, vol. 76, No. 3, 1993, pp. 191-194.

Urakami, T., et al., "Transfer of *Pseudomonas aminovorans* (den Dooren de Jong 1926) to *Aminobacter* gen. nov. as *Aminobacter aminovorans* comb. nov. and Description of *Aminobacter aganoensis* sp. nov. and *Aminobacter niigataensis* sp. nov.", *International Journal of Systematic Bacteriology*, vol. 42, No. 1, Jan. 1992, pp. 84-92.

Venturoli et al., *Biochimica et Biophysica Acta*, 935 (1988) pp. 258-272.

Wakabayashi et al., *Biol. Pharm. Bull*., 1994, 17(8):997-1002.

Wakao, N. et al., "*Acidiphilium multivorm* sp. nov., an Acidophilic Chemoorganotrophic Bacterium from Pyritic Acid Mine Drainage", *Journal of General and Applied Microbiology*, vol. 40, No. 2, 1994, pp. 143-159.

Yabuuchi, E., et al., "Proposals of *Sphingomonas paucimobilis* gen. nov. and comb. nov., *Sphingomonas parapaucimobilis* sp. nov., *Sphingomonas yanoikuyae* sp. nov., *Sphingomonas adhaesiva* sp. nov., *Sphingomonas capsulata* comb. nov., and Two Genospecies of the Genus *Sphingomonas," Microbiology and Immunology*, vol. 34, No. 2, 1990, pp. 99-119.

Yamada, Y., et al., "The Coenzyme Q System in Strains of *Trichosporon* Species and Related Organisms", *Journal of General and Applied Microbiology*, vol. 28, No. 4, 1982, pp. 355-358.

Yoshida, H. et al. "Production of Ubiquinone-10-Using Bacteria", *Journal of General and Applied Microbiology*, vol. 44, No. 1, 1998, pp. 19-26.

* cited by examiner

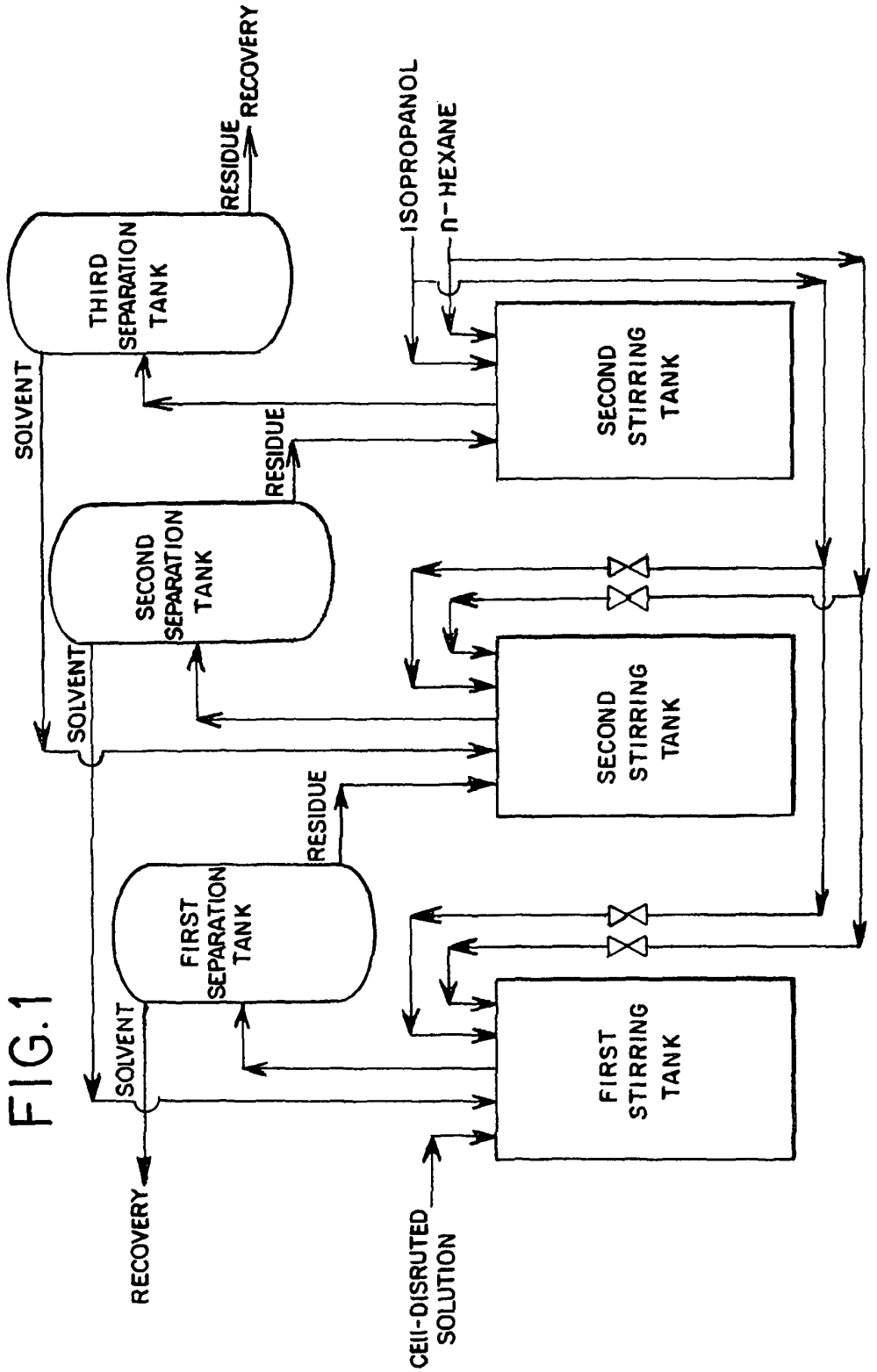

RECOVERY
RESIDUE
THIRD SEPARATION TANK
ISOPROPANOL
n-HEXANE
SOLVENT
SECOND STIRRING TANK
RESIDUE
SECOND SEPARATION TANK
SOLVENT
SECOND STIRRING TANK
RESIDUE
FIRST SEPARATION TANK
SOLVENT
FIRST STIRRING TANK
RECOVERY
CELL-DISRUTED SOLUTION

FIG. 1

PROCESSES FOR PRODUCING COENZYME Q10

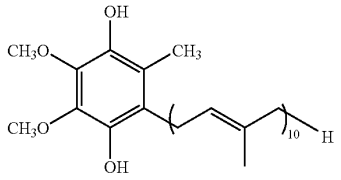
RELATED APPLICATIONS

This application si a divisional of Ser. No. 10/500,249, filed on Nov. 3, 2004 and now abandoned, which is a 371 of PCT/JP02/13766, filed on Dec. 27, 2002, which claims benefits to Japanese Application No. 2001-398545, filed on Dec. 27, 2001.

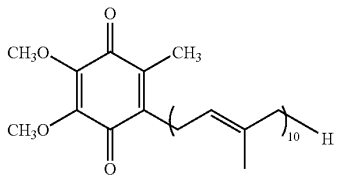
TECHNICAL FIELD

The present invention relates to

a process for producing the reduced coenzyme Q_{10} represented by the following formula (I):



and a process for producing the oxidized coenzyme Q_{10} represented by the following formula (II):



More particularly, the present invention relates to

a process for producing reduced coenzyme Q_{10}

which comprises culturing reduced coenzyme Q_{10}-producing microorganisms to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10},

optionally disrupting the microbial cells and recovering thus-produced reduced coenzyme Q_{10}.

The present invention also relates to a process for producing oxidized coenzyme Q_{10} which comprises either recovering oxidized coenzyme Q_{10} after oxidizing the above-mentioned microbial cells or disrupted product thereof, or recovering reduced coenzyme Q_{10} from the above-mentioned microbial cells or disrupted product thereof to oxidize thus-obtained reduced coenzyme Q_{10} thereafter.

BACKGROUND ART

The reduced coenzyme Q_{10} (I) and the oxidized coenzyme Q_{10} (II) are mitochondrial electron transport system-constituting factors in cells of a living body of human and deal with ATP production by working as electron carriers in oxidative phosphorization reactions.

Conventionally, oxidized coenzyme Q_{10} has been widely used for supplementary nutrient foods and cosmetic products

in addition to pharmaceutical products as a pharmaceutically and physiologically effective substance for a variety of diseases.

On the other hand, reduced coenzyme Q_{10} has not so much drawn attention so far; however, in these years, there has been reported that reduced coenzyme Q_{10} is more effective in various applications than oxidized coenzyme Q_{10}.

For example, Japanese Kokai Publication Hei-10-330251 discloses an antihypercholesterolemia agent having excellent cholesterol reducing function, an antihyperlipemia agent, and an agent for curing and preventing arteriosclerosis which contain reduced coenzyme Q_{10} as an active ingredient. In addition, Japanese Kokai Publication Hei-10-109933 discloses a pharmaceutical composition excellent in oral absorbability comprising coenzyme Q_{10} including reduced coenzyme Q_{10} as an active ingredient.

Furthermore, reduced coenzyme Q_{10} is effective as an antioxidant and a radical scavenger. R. Stocker, et al. have reported that reduced coenzyme Q_{10} prevented peroxidation of human LDL more efficiently than α-tocopherol, lycopene and β-carotene (Proceedings of the National Academy of Science of the United States of America, vol. 88, pp. 1646-1650, 1991).

It has been known that oxidized coenzyme Q_{10} and reduced coenzyme Q_{10} are in a certain type of equilibrium in a living body and that oxidized coenzyme Q_{10}/reduced coenzyme Q_{10} absorbed in the living body are mutually reduced/oxidized.

Reduced coenzyme Q_{10} is supposedly produced by a chemical synthesis method, similarly to the process for producing oxidized coenzyme Q_{10}. But the synthesis process is supposed to be complicated, risky and costly. Moreover, in the case of chemical synthesis methods, it will be necessary to minimize the subgeneration and contamination of a (Z)-isomer, which is suspiciously unsafe (Biomedical and Clinical Aspects of Coenzyme Q, vol. 3, pp. 19-30, 1981). Europe Pharmacopoeia regulates that a content of (Z)-isomer in oxidized coenzyme Q_{10} must be not more than 0.1%.

As another process for producing reduced coenzyme Q_{10}, it can be supposed a method of utilizing microbial cells, that is, a method for separating and recovering reduced coenzyme Q_{10} from reduced coenzyme Q_{10}-producing microorganisms. However, the reduced coenzyme Q_{10} produced by the microbial cells of the above-mentioned microorganisms contains a large amount of oxidized coenzyme Q_{10}, and the separation and recovery of reduced coenzyme Q_{10} by a conventional method results in high cost.

The following are documents describing the presence of reduced coenzyme Q_{10} in microbial cells and there have been known the following examples of bacteria.

(1) An example describing that at lowest 5 to 10% by weight and at highest 30 to 60% by weight of reduced coenzyme Q_{10} are present among the entire coenzymes Q_{10} in culture cells of photosynthesis bacteria (Japanese Kokai Publication Sho-57-70834).

(2) An example describing that the genus *Pseudomonas* is subjected to thermal extraction by an organic solvent in the presence of sodium hydroxide and pyrogallol, and the resultant is treated with 5% sodium hydrosulfite solution, and further dehydrated and concentrated to collect an acetone-soluble portion, and an oil containing reduced coenzyme Q_{10} is obtained (Japanese Kokai Publication Sho-60-75294).

Both of the above (1) and (2) aim to convert a mixture of the obtained reduced coenzyme Q_{10} and oxidized coenzyme Q_{10} or the obtained reduced coenzyme Q_{10} into oxidized coenzyme Q_{10} by further oxidation. Thus, reduced coenzyme Q_{10} is only described as an intermediate substance in producing oxidized coenzyme Q_{10}.

In the above (1), photosynthesis bacteria are used, the culture of which is complicated. Furthermore, in the microbial cells of the above-mentioned microorganisms, when the production of reduced coenzyme Q_{10} is aimed at, it cannot be said that the ratio of reduced coenzyme Q_{10} among the entire coenzymes Q_{10} is sufficient.

The above (2) comprises a process of converting oxidized coenzyme Q_{10} contained in a hexane phase into reduced coenzyme Q_{10} by sodium hydrosulfite, a reducing agent (see Example 3 in Japanese Kokai Publication Sho-60-75294). Thus, the ratio of reduced coenzyme Q_{10} among the entire coenzymes Q_{10} in the microbial cells is not clear.

Furthermore, in both of the above (1) and (2), the production amount of coenzymes Q in culture are not described.

As described above, microbial cells containing reduced coenzyme Q_{10} at high ratio have not been reported yet. Still less, it has not been known a fermentation production of reduced coenzyme Q_{10} on the industrial scale, that is, a method comprising culturing microorganisms to obtain microbial cells containing reduced coenzyme Q_{10} at high ratio among the entire coenzymes Q_{10}, and recovering reduced coenzyme Q_1 to obtain high-purity reduced coenzyme Q_{10}.

Under such circumstances, if a method for obtaining a large quantity of coenzyme Q_{10} containing reduced coenzyme Q_{10} at high ratio by culturing microorganisms is found, it can be a highly useful method for producing reduced coenzyme Q_{10}.

SUMMARY OF THE INVENTION

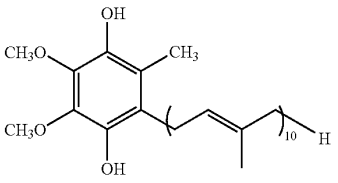
It is an object of the present invention to provide a process for producing reduced coenzyme Q_{10} safely and efficiently on the industrial scale by culturing reduced coenzyme Q_{10}-producing microorganisms for obtaining microbial cells containing reduced coenzyme Q_{10} at high ratio and suitably recovering reduced coenzyme Q_{10} from the microbial cells.

It is another object of the present invention to provide a process for producing oxidized coenzyme Q_{10} in simple processes by culturing reduced coenzyme Q_{10}-producing microorganisms for obtaining microbial cells containing reduced coenzyme Q_{10} at high ratio, and oxidizing the reduced coenzyme Q_{10} obtained from the microbial cells as an intermediate substance in producing oxidized coenzyme Q_{10}.

That is, the present invention relates to

a process for producing the reduced coenzyme Q_{10} represented by the following formula (I):

(I)



which comprises culturing reduced coenzyme Q_{10}-producing microorganisms in a culture medium containing a carbon source, a nitrogen source, a phosphorus source and a micronutrient to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10},

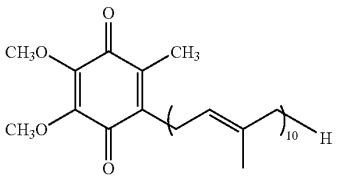
optionally disrupting the microbial cells and

extracting thus-produced reduced coenzyme Q_{10} by an organic solvent.

Furthermore, the present invention also relates to

a process for producing the oxidized coenzyme Q_{10} represented by the following formula (II):

(II)



which comprises culturing reduced coenzyme Q_{10}-producing microorganisms in a culture medium containing a carbon source, a nitrogen source, a phosphorus source and a micronutrient to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10},

optionally disrupting the microbial cells; and

either oxidizing thus-produced reduced coenzyme Q_{10} to oxidized coenzyme Q_{10} and then extracting the resultant by an organic solvent, or extracting thus-produced reduced coenzyme Q_{10} by an organic solvent, purifying optionally and oxidizing the resultant to oxidized coenzyme Q_{10}.

According to the processes of the present invention, reduced coenzyme Q_{10} can be produced cheaply on the industrial scale by considerably simple steps comprising culturing microorganisms and recovering reduced coenzyme Q_{10}. In addition, oxidized coenzyme Q_{10} can also be produced by simple processes. Moreover, these coenzymes Q_{10} produced by microorganisms basically do not contain (Z)-isomers thereof, and (all-E) isomers thereof can be obtained, which are same as those contained in meat, fish, etc.

DETAILED DESCRIPTION OF THE INVENTION

In the present invention, at first, reduced coenzyme Q_{10}-producing microorganisms are cultured to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole %, preferably not less than 75 mole %, among the entire coenzymes Q_{10} (fermentation).

The microbial cells containing reduced coenzyme Q_{10} at such high ratio among the entire coenzymes Q_{10} can be basically obtained by culturing microorganisms capable of producing reduced coenzyme Q_{10} at a ratio of not less than 70 mole %, preferably not less than 75 mole %, among the entire coenzymes Q_{10}.

How much ratio the microorganisms can produce reduced coenzyme Q_{10} among the entire coenzymes Q_{10} can be evaluated, for example, by a method comprising culturing the microorganisms with shaking (amplitude: 2 cm, 310 reciprocation/min) at 25° C. for 72 hours in 10 mL of a culture medium [(glucose: 20 g, peptone: 5 g, yeast extract: 3 g, malt extract: 3 g)/L, pH: 6.0] using a test tube (inner diameter: 21 mm, entire length: 200 mm).

Although the preferable culture conditions for the fermentation production on the industrial scale will be described later, the above-mentioned culture condition is one method for standardizing the ratio of reduced coenzyme Q_{10} produced, which microorganisms have as its ability, so as to reflect the ratio within the range without having significant inaccuracies.

Under the above-mentioned culture condition, it is preferable to use microbial cells wherein a content of reduced

coenzyme Q_{10} is at a ratio of not less than 70 mole %, preferably not less than 75 mole %, among the entire coenzymes Q_{10}, for the present invention. It is still more preferable to use microorganisms having a productivity of reduced coenzyme Q_{10} per unit culture medium of generally not less than 1 μg/mL, preferably not less than 2 μg/mL under the above-mentioned culture condition.

The above-mentioned content of reduced coenzyme Q_{10} and ratio of reduced coenzyme Q_{10} among the entire coenzymes Q_{10} can be confirmed by physically disrupting the microbial cells, extracting coenzyme Q_{10} from thus-obtained cells by an organic solvent and performing HPLC analysis. Specifically, the measurement can be carried out according to the following procedures:

(1) The broth of microorganism is optionally concentrated, 10 parts by volume of the broth are displaced to a screw cap test tube (inner diameter: 16.5 mm, entire length: 130 mm), and 10 parts by volume of glass beads are added (425 to 600 μm, manufactured by SIGMA Co.);

(2) 3 parts by volume of isopropanol and 18.5 parts by volume of n-hexane relative to 10 parts by volume of the broth are added under a nitrogen atmosphere;

(3) microbial cell disruption and extraction are carried out by vigorously shaking of the mixture for 3 minutes under a nitrogen atmosphere; and

(4) the obtained hydrophobic organic solvent phase (n-hexane phase) is evaporated (bath temperature: 40° C.) under reduced pressure to analyze the resultant by HPLC.

Column: YMC-Pack 4.6×250 mm (manufactured by YMC. Co., Ltd.)
Mobile phase: methanol/n-hexane=85/15
Flow rate: 1 mL/min,
Detection: UV 275 nm
Retention time: reduced coenzyme Q_{10} 13.5 min
oxidized coenzyme Q_{10} 22.0 min

The above-mentioned measurement method is provided for the obtained result to reflect the reduced coenzyme Q_{10} content and the ratio of reduced coenzyme Q_{10} among the entire coenzymes Q_{10} as accurate as possible, and to standardize the content and the ratio of reduced coenzyme Q_{10}, which can be guaranteed at the minimum. This method has been demonstrated, by several experimentations performed by the present inventors, easy and suitable to be carried out.

As the above-mentioned reduced coenzyme Q_{10}-producing microorganisms to be used in the present invention, bacteria, yeast and fungi may be used without any specific limitation. As specific examples of the above-mentioned microorganisms, there may be mentioned, for example, microorganisms of the genus *Agrobacterium*, the genus *Aspergillus*, the genus *Acetobacter*, the genus *Aminobacter*, the genus *Agromonas*, the genus *Acidiphilium*, the genus *Bulleromyces*, the genus *Bullera*, the genus *Brevundimonas*, the genus *Cryptococcus*, the genus *Chionosphaera*, the genus *Candida*, the genus *Cerinosterus*, the genus *Exisophiala*, the genus *Exobasidium*, the genus *Fellomyces*, the genus *Filobasidiella*, the genus *Filobasidium*, the genus *Geotrichum*, the genus *Graphiola*, the genus *Gluconobacter*, the genus *Kockovaella*, the genus *Kurtzmanomyces*, the genus *Lalaria*, the genus *Leucosporidium*, the genus *Legionella*, the genus *Methylobacterium*, the genus *Mycoplana*, the genus *Oosporidium*, the genus *Pseudomonas*, the genus *Psedozyma*, the genus *Paracoccus*, the genus *Petromyces*, the genus *Rhodotorula*, the genus *Rhodosporidium*, the genus *Rhizomonas*, the genus *Rhodobium*, the genus *Rhodoplanes*, the genus *Rhodopseudomonas*, the genus *Rhodobacter*, the genus *Sporobolomyces*, the genus *Sporidiobolus*, the genus *Saitoella*, the genus *Schizosaccharomyces*, the genus *Sphingomonas*, the genus *Sporotrichum*, the genus *Sympodiomycopsis*, the genus *Sterigmatosporidium*, the genus *Tapharina*, the genus *Tremella*, the genus *Trichosporon*, the genus *Tilletiaria*, the genus *Tilletia*, the genus *Tolyposporium*, the genus *Tilletiopsis*, the genus *Ustilago*, the genus *Udeniomyces*, the genus *Xanthophilomyces*, the genus *Xanthobacter*, the genus *Paecilomyces*, the genus *Acremonium*, the genus *Hyhomonus*, and the genus *Rhizobium*.

In terms of the culture easiness and productivity, bacteria (preferably nonphotosynthetic bacteria) and yeast are preferred. As the bacteria, there may be mentioned, for example, the genus *Agrobacterium*, the genus *Gluconobacter* and the like. As the yeast, there may be mentioned, for example, the genus *Schizosaccharomyces*, the genus *Saitoella* and the like.

As preferable species, there may be mentioned, for example, *Agrobacterium tumefacience* IFO13263, *Agrobacterium radiobacter* ATCC4718, *Aspergillus clavatus* JCM1718, *Acetobacter xylinum* IFO15237, *Aminobacter aganouensis* JCM7854, *Agromonas oligotrophica* JCM1494, *Acidiphilium multivorum* JCM8867, *Bulleromyces albus* IFO1192, *Bullera armeniaca* IFO10112, *Brevundimonas diminuta* JCM2788, *Cryptococcus laurentii* IFO0609, *Chionosphaera apobasidialis* CBS7430, *Candida curvata* ATCC10567, *Cerinosterus luteoalbus* JCM2923, *Exisophiala alcalophila* JCM12519, *Exobasidium gracile* IFO7788, *Fellomyces fuzhouensis* IFO10374, *Filobasidiella neoformans* CBS132, *Filobasidium capsuloigenum* CBS1906, *Geotrichum capitatum* JCM6258, *Graphiola cylindrica* IFO6426, *Gluconobacter suboxydans* IFO3257, *Kockovaella imperatae* JCM7826, *Kurtzmanomyces nectairei* IFO10118, *Lalaria cerasi* CBS275.28, *Leucosporidium scottii* IFO1212, *Legionella anisa* JCM7573, *Methylobacterium extorguens* JCM2802, *Mycoplana ramosa* JCM7822, *Oosporidium margaritiferum* CBS2531, *Pseudomonas denitrificans* IAM 12023, *Pseudomonas shuylkilliensis* IAM 1092, *Psedozyma aphidis* CBS517.23, *Paracoccus denitrificans* JCM6892, *Petromyces alliaceus* IFO7538, *Rhodotorula glutinis* IFO1125, *Rhodotorula minuta* IFO0387, *Rhodosporidium diobovatum* ATCC1830, *Rhizomonas suberifaciens* IFO15212, *Rhodobium orients* JCM9337, *Rhodoplanes elegans* JCM9224, *Rhodopseudomonas palustris* JCM2524, *Rhodobacter capsulatus* SB1003, *Sporobolomyces holsaticus* IFO1034, *Sporobolomyces pararoseus* IFO0471, *Sporidiobolus johnsonii* IFO1840, *Saitoella complicata* IFO10748, *Schizosaccharomyces pombe* IFO0347, *Sphingomonas parapaucimobilis* IFO15100, *Sporotrichum cellulophilium* ATCC20493, *Sympodiomycopsis paphiopedili* JCM8318, *Sterigmatosporidium polymorphum* IFO10121, *Sphingomonas adhesiva* JCM7370, *Tapharina caerulescens* CBS351.35, *Tremella mesenterica* ATCC24438, *Trichosporon cutaneum* IFO1198, *Tilletiaria anomala* CBS436.72, *Tilletia caries* JCM1761, *Tolyposporium bullatum* JCM2006, *Tilletiopsis washintonesis* CBS544, *Ustilago esculenta* IFO9887, *Udeniomyces megalosporus* JCM5269, *Xanthophilomyces dendrorhous* IFO10129, *Xanthobacter flavus* JCM1204, *Paecilomyces lilacinus* ATCC10114, *Acremonium chrysogenum* ATCC11550, *Hyphomonas hirschiana* ATCC33886, *Rhizobium meliloti* ATCC9930, and the like.

As the reduced coenzyme Q_{10}-producing microorganisms, not only the wild species of the above-mentioned microorganisms but also microorganisms in which the transcription and translation activities of the genes relevant to the biosynthesis of reduced coenzyme Q_{10} in the above-mentioned microorganisms, or the enzyme activity of the expressed protein are modified or improved can be used preferably, for example.

As the means for modifying or improving the transcription and translation activities of the genes or the enzyme activity of the expressed protein, there may be mentioned gene recombination (including gene improvement, amplification and destruction by itself, external gene introduction, and gene improvement and proliferation of thus-introduced external genes) and mutagenesis by mutagens. In particular, the mutagenesis by mutagens is preferred.

The more preferable microorganisms usable for the present invention are microorganisms containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole %, preferably not less than 75 mole %, more preferably not less than 80 mole %, still more preferably not less than 85 mole %, and particularly preferably not less than 90 mole %, among the entire coenzymes Q_{10} in the case where the above-mentioned modified or improved microorganisms, preferably microorganisms mutated by mutagens, are evaluated by the above-mentioned proliferation method and the measurement method. In the fermentation production on the industrial scale, it is preferable to use microorganisms having a productivity of reduced coenzyme Q_{10} per unit culture medium of not less than 1 μg/mL, preferably not less than 2 μg/mL, more preferably not less than 3 μg/mL, still more preferably not less than 5 μg/mL, particularly preferably not less than 10 μg/mL, much more preferably not less than 15 μg/mL, and most preferably not less than 20 μg/mL.

The mutagenesis may be carried out by a single mutagenesis; however, mutagenesis is preferably carried out not less than 2 times. That is because it was found that the productivity of reduced coenzyme Q_{10} can be improved in the respective mutagenesis steps. It is needless to say that the candidates of the microbial cells to be mutated are, generally, those having a productivity of reduced coenzyme Q_{10} as high as possible in the case where the evaluation is carried out by the above-mentioned proliferation method and measurement method.

The mutagenesis can be carried out by using optional and proper mutagens. The term "mutagen" encompasses, in a board definition, not only chemical agents having mutagenesis effects, for example, but also treatments such as UV radiation having mutagenesis effects. As examples of proper mutangens, there may be mentioned ethyl methanesulfonate, UV radiation, N-methyl-N'-nitro-N-nitrosoguanidine, nucleotide base analogues such as bromouracil, and acridines; however, they are not limited to these examples.

According to a conventional mutagenesis technique, successively to the mutagenesis, a proper selection of microbial cells having high productivity of reduced coenzyme Q_{10} is carried out. For that, the culture obtained from a single colony should be evaluated, for example, by the above-mentioned proliferation method and measurement method. Since a reduced coenzyme Q_{10} crystal forms a white solid layer or a colorless liquid phase, a productivity of reduced coenzyme Q_{10} can be suitably evaluated by the above-mentioned measurement method at the time of selection of the colony.

In the processes of the present invention, high productivity of reduced coenzyme Q_{10} in the fermentation production on the industrial scale can be achieved partially by using the microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10} and, partially, by using the suitable conditions of culture (fermentation) for increasing a productivity of reduced coenzyme Q_{10} per unit culture medium as described below. It is particularly preferable to combinedly use suitable microbial cells described above and the suitable conditions of culture (fermentation) as described below.

The culture is carried out, in general, in a culture medium containing major nutrients and micronutrients suited for microorganism proliferation. As the above-mentioned nutrients, there may be mentioned, for example, carbon sources (e.g. hydrocarbons such as glucose, sucrose, maltose, starch, corn syrup and molasses; alcohols such as methanol and ethanol), nitrogen sources (e.g. corn steep liquor, ammonium sulfate, ammonium phosphate, ammonium hydroxide, urea and peptone), phosphorus sources (e.g. ammonium phosphate and phosphoric acid) and micronutrients (e.g. minerals such as magnesium, potassium, zinc, copper, iron, manganese, molybdenum, sulfuric acid and hydrochloric acid; vitamins such as biotin, desthiobiotin and vitamin B1; amino acids such as alanine and histidine; and natural raw materials containing vitamins such as yeast extract and malt extract); however, these are not limitative ones, and commonly used ones may be used. Incidentally, in natural components of a culture medium, such as yeast extract, phosphorus sources such as phosphates are contained. The above-mentioned nutrients can be appropriately used in combination.

The culture is generally carried out at a temperature range of 15 to 45° C., preferably 20 to 37° C. If it is below 15° C., the proliferation speed of microorganisms tends to be too slow to allow the industrial production and at high temperatures exceeding 45° C., the viability of microorganisms tends to be easily hindered.

In general, the culture is carried out at a pH range of 4 to 9, preferably 5 to 8. If the pH is not more than 3 or not less than 10, proliferation of microorganisms tends to be easily inhibited.

In the fermentation production on the industrial scale, although it depends on the microorganism species, the concentration of the carbon sources (including the produced alcohols) during the culture is preferably controlled to a concentration that no adverse effects are substantially caused on the productivity of reduced coenzyme Q_{10}. Accordingly, it is preferable to control the culture so as to have the concentration of the carbon sources that no adverse effects are substantially caused on the productivity of reduced coenzyme Q_{10}, that is, generally to not more than 20 g/L, preferably not more than 5 g/L, and more preferably not more than 2 g/L in the broth.

To control the concentration of the carbon sources, a fed batch culture method is preferably used. The carbon source concentration in the broth can be controlled by adjusting the supply of nutrient sources (especially carbon sources) based on the culture control indexes such as pH, the dissolved oxygen concentration (DO) or the remaining saccharide concentration. Although it depends on the microorganism species, the supply of the nutrient sources may be started from the initial stage of the culture or during the culture. The supply of the nutrient sources may be continuous or intermittent. Incidentally, in supplying the nutrient sources, it is preferable to supply the above-mentioned carbon sources to the culture medium separately from other components.

The culture can be completed at the point when a desired amount of reduced coenzyme Q_{10} is produced. The culture duration is not particularly limited and it is generally 20 to 200 hours.

The above-mentioned culture is generally carried out aerobically. The term "aerobically" means a condition that oxygen is supplied so as not to cause oxygen limitation (oxygen deficiency) during the culture, and preferably a condition that oxygen is supplied sufficiently so as not to cause substantial oxygen limitation during the culture. The culture is carried out generally under an aeration condition, preferably under an aeration and stirring condition.

By using the above-mentioned microorganisms and culture conditions, it becomes possible to obtain microbial cells

containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole %, preferably not less than 75 mole % among the entire coenzymes Q_{10}. Furthermore, the productivity of reduced coenzyme Q_{10} of as high as not less than 1 μg/mL, preferably not less than 2 μg/mL, and still more preferably not less than 3 μg/mL can be obtained.

Next, recovery of the reduced coenzyme Q_{10} produced by the above-mentioned culture will be described.

In the present invention, an efficient production of reduced coenzyme Q_{10} on the industrial scale is made to be possible partially by the above-mentioned suitable culture and partially by the suitable recovery process of reduced coenzyme Q_{10} as described below.

Recovery of reduced coenzyme Q_{10} is carried out by extraction from the microbial cells obtained by the above-mentioned culture using an organic solvent.

In the extraction, cells can be disrupted optionally. The cell disruption contributes to the efficient extraction of the reduced coenzyme Q_{10} produced and accumulated in cells. It is needless to say that the cell disruption and extraction can be carried out at the same time.

Incidentally, "disruption" in the present invention may be carried out to the extent that the surface structure such as a cell wall is broken so as to make extraction of reduced coenzyme Q_{10} possible; therefore, it is not necessary that microbial cells are torn or fragmentated.

The above-mentioned cell disruption is not necessarily required in the case of bacteria. However, in the case of yeast or fungi, the cell disruption is generally required and, when cells are not disrupted, it becomes difficult to efficiently recover the reduced coenzyme Q_{10} produced and accumulated in the cells.

The above-mentioned disruption of microbial cells can be carried out by the following one or several disruption methods in optional order. As the disruption method, there may be mentioned, for example, a physical treatment, a chemical treatment, an enzymic treatment as well as a heating treatment, an autolysis, an osmolysis, a plasmoptysis and the like.

The above-mentioned physical treatment can be carried out, for example, by using a high pressure homogenizer, an ultrasonic homogenizer, a French press, a ball mill and the like or using them in combination.

The above-mentioned chemical treatment can be carried out, for example, by using an acid (preferably a strong acid) such as hydrochloric acid and sulfuric acid, a base (preferably a strong base) such as sodium hydroxide and potassium hydroxide and the like or using them in combination.

The above-mentioned enzymic treatment can be carried out, for example, by using lysozyme, zymolyase, glucanase, Novozyme, protease, cellulase and the like or by using them appropriately in combination.

The above-mentioned heating treatment can be carried out, for example, by heating to the temperature range of 60 to 100° C. for about 30 minutes to 3 hours.

The above-mentioned autolysis can be carried out, for example, by treatment with a solvent such as ethyl acetate.

The osmolysis or the plasmoptysis for disrupting cells by treating cells with a solution having a different salt concentration from that in the cells are often combinedly used with the above-mentioned physical treatment, chemical treatment, enzymic treatment, heating treatment, autolysis and/or the like since the above lytic method alone is insufficient in the disruption effect.

As the cell disruption method as a pretreatment of extraction and recovery of reduced coenzyme Q_{10}, among the above-mentioned disruption methods, the physical treatment, the chemical treatment (particularly, an acid treatment and preferably the one with a strong acid (e.g. an acid having a pKa value of not more than 2.5 in the form of an aqueous solution) under the condition that reduced coenzyme Q_{10} is protected from an oxidation reaction as described below) and the heating treatment are preferred. From the viewpoint of disruption efficiency, the physical treatment is more preferred.

A conventional cell disruption method and coenzyme Q_{10} extraction method, specifically, a method comprising extracting coenzyme Q_{10} by an organic solvent in the presence of sodium hydroxide and pyrogallol has problems in terms of cost, waste treatment, safety in effective utilization of waste microorganisms (waste cells) such as recovery of protein, and the like. However, the cell disruption method, particularly the physical treatment method of the present invention, does not cause subgeneration of a large quantity of salts by neutralization, and is a suitable method from a viewpoint of the waste treatment and the effective utilization of waste microorganisms (waste cells).

The form of the microbial cells to be used for the above-mentioned cell disruption may be a broth, a concentrated broth, microbial cells collected as wet cells from the broth, a product obtained by washing them, a suspension of the wet cells in a solvent (including, for example, water, physiological saline solution, buffers and the like), dry cells obtained by drying the above-mentioned wet cells, a suspension of the dry cells in a solvent (including, for example, water, physiological saline solution, buffers and the like), and the like. Preferred is an aqueous suspension of microbial cells, and in terms of operability and the like, more preferred are the broth, the concentrated broth, and the product obtained by washing them.

The form of the above-mentioned microbial cells or disrupted product thereof to be used for extraction and recovery of reduced coenzyme Q_{10} is, similarly as described above, not particularly limited and may be wet cells/dry cells of the microbial cells/disrupted product thereof. Preferably, it is an aqueous suspension of the microbial cells or disrupted product thereof, and more preferably the broth, the concentrated and/or washed broth, or solutions obtained by disrupting them (each of them is an aqueous suspension).

The cell concentration in the above-mentioned suspension of the microbial cells or disrupted product thereof is not particularly limited and is generally 1 to 25% by weight on the basis of dry weight. Preferably, it is 10 to 20% by weight in terms of cost.

Reduced coenzyme Q_{10} can be recovered by extracting the microbial cells and disrupted product thereof obtained in such a manner by an organic solvent.

As the organic solvent to be used for the extraction, there may be mentioned hydrocarbons, fatty acid esters, ethers, alcohols, fatty acids, ketones, nitrogen compounds (including nitrites and amides), sulfur compounds and the like.

Particularly, in extracting reduced coenzyme Q_{10}, in terms of protection from oxidation by a molecular oxygen, at least one species of hydrocarbons, fatty acid esters, ethers, and nitrites is preferably used. Among them, hydrocarbons and fatty acid esters are particularly preferable, and hydrocarbons are most preferable.

On the industrial production scale, complete oxygen elimination is very difficult to be achieved and, furthermore, fairly long periods of time are required for individual operations, unlike laboratory scale production, so that residual oxygen exerts a great adverse effect. The oxidation in question is directly connected to a subgeneration of oxidized coenzyme Q_{10} from reduced coenzyme Q_{10}. Accordingly, use of the above-mentioned organic solvent (such as hydrocarbons,

fatty acid esters, ethers, and nitrites) with high oxidation prevention effect in the extraction of reduced coenzyme Q_{10} assists an efficient extraction.

The hydrocarbons are not particularly restricted, but there may be mentioned, for example, aliphatic hydrocarbons, aromatic hydrocarbons, halogenated hydrocarbons, and the like. Preferred are aliphatic hydrocarbons and aromatic hydrocarbons, and more preferred are aliphatic hydrocarbons.

The aliphatic hydrocarbons are not particularly restricted, and may be cyclic or acyclic, or saturated or unsaturated. However, generally, saturated ones are preferably used. Usually, ones containing 3 to 20 carbon atoms, preferably 5 to 12 carbon atoms, and more preferably 5 to 8 carbon atoms are used. As specific examples, there may be mentioned, for example, propane, butane, isobutane, pentane, 2-methylbutane, hexane, 2-methylpentane, 2,2-dimethylbutane, 2,3-dimethylbutane, heptane, heptane isomers (e.g. 2-methylhexane, 3-methylhexane, 2,3-dim-ethylpentane, 2,4-dimethylpentane), octane, 2,2,3-trimethylpentane, isooctane, nonane, 2,2,5-trimethylhexane, decane, dodecane, 2-pentene, 1-hexene, 1-heptene, 1-octene, 1-nonene, 1-decene, cyclopentane, methylcyclopentane, cyclohexane, methylcyclohexane, ethylcyclohexane, p-menthane, cyclohexene, and the like. Preferred are pentane, 2-methylbutane, hexane, 2-methylpentane, 2,2-dimethylbutane, 2,3-dimethylbutane, heptane, heptane isomers (e.g. 2-methylhexane, 3-methylhexane, 2,3-dimethylpentane, 2,4-dimethylpentane), octane, 2,2,3-trimethylpentane, isooctane, nonane, 2,2,5-trimethylhexane, decane, dodecane, cyclopentane, methylcyclopentane, cyclohexane, methylcyclohexane, ethylcyclohexane, p-menthane, and the like. More preferred are pentane, 2-methylbutane, hexane, 2-methylpentane, 2,2-dimethylbutane, 2,3-dimethylbutane, heptane, heptane isomers (e.g. 2-methylhexane, 3-methylhexane, 2,3-dimethylpentane, 2,4-dimethylpentane), octane, 2,2,3-trimethylpentane, isooctane, cyclopentane, methylcyclopentane, cyclohexane, methylcyclohexane, ethylcyclohexane, and the like.

Generally, heptanes, not only heptane but also heptane isomers such as methylcyclohexane having 7 carbon atoms and a mixture thereof are preferably used. More preferred are pentanes (e.g. pentane and the like) having 5 carbon atoms, hexanes (e.g. hexane, cyclohexane and the like) having 6 carbon atoms, and heptanes (e.g. heptane, methylcyclohexane and the like) having 7 carbon atoms. Particularly preferred are heptanes (e.g. heptane, methylcyclohexane and the like) in terms of especially high protection effect from oxidation, and the most preferred is heptane.

The aromatic hydrocarbons are not particularly restricted, but generally ones containing 6 to 20 carbon atoms, preferably 6 to 12 carbon atoms, and more preferably 7 to 10 carbon atoms are used. As specific examples, there may be mentioned, for example, benzene, toluene, xylene, o-xylene, m-xylene, p-xylene, ethylbenzene, cumene, mesitylene, tetralin, butylbenzene, p-cymene, cyclohexylbenzene, diethylbenzene, pentylbenzene, dipentylbenzene, dodecylbenzene, styrene, and the like. Preferred are toluene, xylene, o-xylene, m-xylene, p-xylene, ethylbenzene, cumene, mesitylene, tetralin, butylbenzene, p-cymene, cyclohexylbenzene, diethylbenzene, pentylbenzene and the like. More preferred are toluene, xylene, o-xylene, m-xylene, p-xylene, cumene, tetralin and the like, and most preferred is cumene.

The halogenated hydrocarbons are not particularly restricted, and may be cyclic or acyclic, or saturated or unsaturated. However, acyclic ones are preferably used in general. Usually, more preferred are chlorinated hydrocarbons and fluorinated hydrocarbons, and chlorinated hydrocarbons are still more preferred. Additionally, ones containing 1 to 6 carbon atoms, preferably 1 to 4 carbon atoms, and more preferably 1 to 2 carbon atoms are suitably used. As specific examples, for example, there may be mentioned dichloromethane, chloroform, carbon tetrachloride, 1,1-dichloroethane, 1,2-dichloroethane, 1,1,1-trichloroethane, 1,1,2-trichloroethane, 1,1,1,2-tetrachloroethane, 1,1,2,2-tetrachloroethane, pentachloroethane, hexachloroethane, 1,1-dichloroethylene, 1,2-dichloroethylene, trichloroethylene, tetrachloroethylene, 1,2-dichloropropane, 1,2,3-trichloropropane, chlorobenzene, 1,1,1,2-tetrafluoroethane, and the like. Preferred are dichloromethane, chloroform, carbon tetrachloride, 1,1-dichloroethane, 1,2-dichloroethane, 1,1,1-trichloroethane, 1,1,2-trichloroethane, 1,1-dichloroethylene, 1,2-dichloroethylene, trichloroethylene, chlorobenzene, 1,1,1,2-tetrafluoroethane, and the like. More preferred are dichloromethane, chloroform, 1,2-dichloroethylene, trichloroethylene, chlorobenzene, 1,1,1,2-tetrafluoroethane and the like.

The fatty acid esters are not particularly restricted, but there may be mentioned, for example, propionates, acetates, formates, and the like. Preferred are acetates and formates, and more preferred are acetates. Ester functional groups thereof are not particularly restricted, but, in general, preferred are alkyl esters having 1 to 8 carbon atoms and aralkyl esters having 7 to 12 carbon atoms, more preferred are alkyl esters having 1 to 6 carbon atoms, and still more preferred are alkyl esters having 1 to 4 carbon atoms.

As specific examples of the propionates, there may be mentioned, for example, methyl propionate, ethyl propionate, butyl propionate, isopentyl propionate, and the like. Preferred are ethyl propionate and the like.

As specific examples of the acetates, there may be mentioned, for example, methyl acetate, ethyl acetate, propyl acetate, isopropyl acetate, butyl acetate, isobutyl acetate, sec-butyl acetate, pentyl acetate, isopentyl acetate, sec-hexyl acetate, cyclohexyl acetate, benzyl acetate, and the like. Preferred are methyl acetate, ethyl acetate, propyl acetate, isopropyl acetate, butyl acetate, isobutyl acetate, sec-butyl acetate, pentyl acetate, isopentyl acetate, sec-hexyl acetate, cyclohexyl acetate, and the like. More preferred are methyl acetate, ethyl acetate, propyl acetate, isopropyl acetate, butyl acetate, isobutyl acetate, and the like. Most preferred is ethyl acetate.

As specific examples of the formates, there may be mentioned, for example, methyl formate, ethyl formate, propyl formate, isopropyl formate, butyl formate, isobutyl formate, sec-butyl formate, pentyl formate, and the like. Preferred are methyl formate, ethyl formate, propyl formate, butyl formate, isobutyl formate, pentyl formate, and the like. Most preferred is ethyl formate.

The ethers are not particularly restricted, and may be cyclic or acyclic, or saturated or unsaturated. But saturated ones are preferably used in general. Generally, ones containing 3 to 20 carbon atoms, preferably 4 to 12 carbon atoms and more preferably 4 to 8 carbon atoms are used. As specific examples, there may be mentioned, for example, diethyl ether, methyl tert-butyl ether, dipropyl ether, diisopropyl ether, dibutyl ether, dihexyl ether, ethyl vinyl ether, butyl vinyl ether, anisol, phenetole, butyl phenyl ether, methoxytoluene, dioxane, furan, 2-methylfuran, tetrahydrofuran, tetrahydropyran, ethylene glycol dimethyl ether, ethylene glycol diethyl ether, ethylene glycol dibutyl ether, ethylene glycol monomethyl ether, ethylene glycol monoethyl ether, ethylene glycol monobutyl ether, and the like. Preferred are diethyl ether, methyl tert-butyl ether, dipropyl ether, diisopropyl ether, dibutyl ether, dihexyl ether, anisol, phenetole, butyl phenyl ether, methoxytoluene, dioxane, 2-methylfuran, tetrahydrofuran, tetrahydropyran, ethylene glycol dimethyl ether, eth-

ylene glycol diethyl ether, ethylene glycol dibutyl ether, ethylene glycol monomethyl ether, ethylene glycol monoethyl ether, and the like. More preferred are diethyl ether, methyl tert-butyl ether, anisol, dioxane, tetrahydrofuran, ethylene glycol monomethyl ether, ethylene glycol monoethyl ether, and the like. Still more preferred are diethyl ether, methyl tert-butyl ether, anisol, and the like, and most preferred is methyl tert-butyl ether.

The alcohols are not particularly restricted but may be cyclic or acyclic, or saturated or unsaturated. Saturated ones are generally preferred, however. Generally, ones containing 1 to 20 carbon atoms, more preferably 1 to 12 carbon atoms, and still more preferably 1 to 6 carbon atoms are used. Among them, monohydric alcohols containing 1 to 5 carbon atoms, dihydric alcohols containing 2 to 5 carbon atoms, and trihydric alcohols containing 3 carbon atoms are preferred.

As specific examples of these alcohols, there may be mentioned, for example, monohydric alcohols such as methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, 2-butanol, isobutyl alcohol, tert-butyl alcohol, 1-pentanol, 2-pentanol, 3-pentanol, 2-methyl-1-butanol, isopentyl alcohol, tert-pentyl alcohol, 3-methyl-2-butanol, neopentyl alcohol, 1-hexanol, 2-methyl-1-pentanol, 4-methyl-2-pentanol, 2-ethyl-1-butanol, 1-heptanol, 2-heptanol, 3-heptanol, 1-octanol, 2-octanol, 2-ethyl-1-hexanol, 1-nonanol, 1-decanol, 1-undecanol, 1-dodecanol, allyl alcohol, propargyl alcohol, benzyl alcohol, cyclohexanol, 1-methylcyclohexanol, 2-methylcyclohexanol, 3-methylcyclohexanol, 4-methylcyclohexanol, and the like; dihydric alcohols such as 1,2-ethanediol, 1,2-propandiol, 1,3-propandiol, 1,2-butanediol, 1,3-butanediol, 1,4-butanediol, 2,3-butanediol, 1,5-pentanediol, and the like; and trihydric alcohols such as glycerol, and the like.

As the monohydric alcohols, preferred are methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, 2-butanol, isobutyl alcohol, tert-butyl alcohol, 1-pentanol, 2-pentanol, 3-pentanol, 2-methyl-1-butanol, isopentyl alcohol, tert-pentyl alcohol, 3-methyl-2-butanol, neopentyl alcohol, 1-hexanol, 2-methyl-1-pentanol, 4-methyl-2-pentanol, 2-ethyl-1-butanol, 1-heptanol, 2-heptanol, 3-heptanol, 1-octanol, 2-octanol, 2-ethyl-1-hexanol, 1-nonanol, 1-decanol, 1-undecanol, 1-dodecanol, benzyl alcohol, cyclohexanol, 1-methylcyclohexanol, 2-methylcyclohexanol, 3-methylcyclohexanol, 4-methylcyclohexanol, and the like. More preferred are methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, 2-butanol, isobutyl alcohol, tert-butyl alcohol, 1-pentanol, 2-pentanol, 3-pentanol, 2-methyl-1-butanol, isopentyl alcohol, tert-pentyl alcohol, 3-methyl-2-butanol, neopentyl alcohol, 1-hexanol, 2-methyl-1-pentanol, 4-methyl-2-pentanol, 2-ethyl-1-butanol, cyclohexanol, and the like. Still more preferred are methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, 2-butanol, isobutyl alcohol, tert-butyl alcohol, 1-pentanol, 2-pentanol, 3-pentanol, 2-methyl-1-butanol, isopentyl alcohol, tert-pentyl alcohol, 3-methyl-2-butanol, neopentyl alcohol, and the like. Particularly preferred are methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, 2-butanol, isobutyl alcohol, 2-methyl-1-butanol, isopentyl alcohol, and the like. Most preferred is 2-propanol.

As the dihydric alcohols, preferred are 1,2-ethanediol, 1,2-propandiol, 1,3-propandiol, and the like. Most preferred is 1,2-ethanediol. As the trihydric alcohols, glycerol is preferred.

As fatty acids, there may be mentioned, for example, formic acid, acetic acid, propionic acid, and the like. Preferred are formic acid and acetic acid, and most preferred is acetic acid.

The ketones are not particularly restricted, and ones having 3 to 6 carbon atoms are preferably used. As specific examples, there may be mentioned, for example, acetone, methyl ethyl ketone, methyl butyl ketone, methyl isobutyl ketone, and the like. Preferred are acetone and methyl ethyl ketone, and most preferred is acetone.

The nitriles are not particularly restricted, and may be cyclic or acyclic, or saturated or unsaturated. However, saturated ones are preferably used in general. Generally, ones containing 2 to 20 carbon atoms, preferably 2 to 12 carbon atoms, and more preferably 2 to 8 carbon atoms are used.

As specific examples, there may be mentioned, for example, acetonitrile, propiononitrile, malononitrile, butyronitrile, isobutyronitrile, succinonitrile, valeronitrile, glutaronitrile, hexanenitrile, heptylcyanide, octylcyanide, undecanenitrile, dodecanenitrile, tridecanenitrile, pentadecanenitrile, stearonitrile, chloroacetonitrile, bromoacetonitrile, chloropropiononitrile, bromopropiononitrile, methoxyacetonitrile, methyl cyanoacetate, ethyl cyanoacetate, tolunitrile, benzonitrile, chlorobenzonitrile, bromobenzonitrile, cyanobenzoic acid, nitrobenzonitrile, anisonitrile, phthalonitrile, bromotolunitrile, methyl cyanobenzoate, methoxybenzonitrile, acetylbenzonitrile, naphthonitrile, biphenylcarbonitrile, phenylpropiononitrile, phenylbutyronitrile, methylphenylacetonitrile, diphenylacetonitrile, naphthylacetonitrile, nitrophenylacetonitrile, chlorobenzylcyanide, cyclopropanecarbonitrile, cyclohexanecarbonitrile, cycloheptanecarbonitrile, phenylcyclohexanecarbonitrile, tolylcyclohexanecarbonitrile, and the like.

Preferred are acetonitrile, propiononitrile, succinonitrile, butyronitrile, isobutyronitrile, valeronitrile, methyl cyanoacetate, ethyl cyanoacetate, benzonitrile, tolunitrile and chloropropiononitrile. More preferred are acetonitrile, propiononitrile, butyronitrile and isobutyronitrile, and most preferred is acetonitrile.

As the nitrogen compounds other than nitriles, there may be mentioned, for example, amides such as formamide, N-methylformamide, N,N-dimethylformamide, N,N-dimethylacetoamide, N-methylpyrrolidone, and nitromethane, triethylamine, pyridine, and the like.

As the sulfur compounds, there may be mentioned, for example, dimethyl sulfoxide, sulfolane, and the like.

In selecting the organic solvent to be used from among the organic solvents mentioned above, such properties as boiling point and viscosity (e.g. the solvent should have a boiling point which allows appropriate warming for increasing solubility and facilitates a solvent removal from wet masses by drying and solvent recovery from crystallization filtrates and the like (about 30 to 150° C. at 1 atm), a melting point such that solidification hardly occurs in handling at room temperature as well as upon cooling to room temperature or below (not lower than about 0° C., preferably not lower than about 10° C., more preferably not lower than about 20° C.), and a low viscosity (not higher than about 10 cp at 20° C. and the like)) are preferably taken into consideration.

The oxidation prevention effect on reduced coenzyme Q_{10} in a solvent tends to increase in a highly-concentrated solution of reduced coenzyme Q_{10}. Reduced coenzyme Q_{10} shows high solubility in the above-mentioned organic solvents with high oxidation prevention effect (e.g. hydrocarbons, fatty acid esters and the like). The high solubility makes it possible to handle the highly-concentrated solution and to promote the oxidation prevention. A preferable concentration of reduced coenzyme Q_{10} for oxidation prevention at the time of extraction is not particularly limited, but is generally not less than 0.001% by weight, preferably not less than 0.01% by weight, and more preferably not less than 0.1% by weight as the concentration of reduced coenzyme Q_{10} in the above-

mentioned organic solvent. The upper limit is not particularly limited, however, in general, it is not more than 10% by weight.

Among the above-mentioned organic solvents, to extract and recover reduced coenzyme Q_{10} from wet cells and dry cells of the microbial cells or disrupted product thereof, hydrophilic organic solvents are preferably used. Specifically, there may be mentioned acetone, acetonitrile, methanol, ethanol, 1-propanol, 2-propanol and the like.

Furthermore, among the above-mentioned organic solvents, to extract and recover reduced coenzyme Q_{10} from the aqueous suspension of the microbial cells or disrupted product thereof, hydrophobic organic solvents are preferably used. Use of such solvents assists the removal of water-soluble substances derived from microorganisms. Many of hydrophobic organic solvents have high oxidation prevention effect as described above, thus are very advantageous.

As the hydrophobic organic solvents, hydrocarbons, fatty acid esters and ethers are preferred.

In the case of the above-mentioned extraction operation, when reduced coenzyme Q_{10} is extracted from the aqueous suspension of the microbial cells or disrupted product thereof, particularly from the aqueous suspension of the disrupted product, further particularly the case in which the disrupted product is physically treated, by an organic solvent, emulsions tend to be partly formed because of the presence of cell components such as proteins and phase separation tends to be difficult. Therefore, it becomes important to suppress the formation of emulsions mentioned above and to efficiently carry out extraction.

For that, as an extraction solvent, in addition to the above-mentioned hydrophobic organic solvent, it is preferable to use a hydrophilic organic solvent as an auxiliary solvent in combination.

In this case, the hydrophobic organic solvent is not particularly limited and those mentioned above may be used. Preferred are hydrocarbons, and more preferred are aliphatic hydrocarbons. Among the aliphatic hydrocarbons, those having 5 to 8 carbon atoms are preferably used.

As specific examples of the aliphatic hydrocarbons containing 5 to 8 carbon atoms, there may be mentioned, for example, pentane, 2-methylbutane, hexane, 2-methylpentane, 2,2-dimethylbutane, 2,3-dimethylbutane, heptane, heptane isomers (e.g. 2-methylhexane, 3-methylhexane, 2,3-dimethylpentane, 2,4-dimethylpentane), octane, 2,2,3-trimethylpentane, isooctane, cyclopentane, methylcyclopentane, cyclohexane, methylcyclohexane, ethylcyclohexane, and the like. Particularly preferred are hexane, heptane and methylcyclohexane, and most preferred are hexane and heptane.

The hydrophilic organic solvent to be used in combination with the above-mentioned hydrophobic organic solvent is not particularly limited and those mentioned above may be used. Preferred are alcohols. Among the alcohols, monohydric alcohols having 1 to 5 carbon atoms are preferably used. As specific examples thereof, there may be mentioned, for example, methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, 2-butanol, isobutyl alcohol, tert-butyl alcohol, 1-pentanol, 2-pentanol, 3-pentanol, 2-methyl-1-butanol, isopentyl alcohol, tert-pentyl alcohol, 3-methyl-2-butanol, neopentyl alcohol, and the like. Particularly preferred are methanol, ethanol, 1-propanol and 2-propanol, and most preferred is 2-propanol.

The amounts of the above-mentioned hydrophilic organic solvent and hydrophobic organic solvent to be used are not particularly limited. But preferably, as the concentration at the time of extraction, the hydrophilic organic solvent is used in a range of 5 to 50% by volume and the hydrophobic organic solvent is used in a range of 25 to 65% by volume relative to the total volume of the entire solution.

In recovering reduced coenzyme Q_{10}, the temperature at the time of extraction is not particularly limited and is generally in a range of 0 to 60° C. and preferably 20 to 50° C.

As the extraction method, both batch extraction and continuous extraction (preferably countercurrent multistage extraction) may be used. However, the continuous extraction (preferably countercurrent multistage extraction) is preferable in terms of productivity. The stirring duration in the batch extraction is not particularly limited but is generally not less than 5 minutes. The average retention time in the continuous extraction is not particularly limited but is generally not less than 10 minutes.

In recovering reduced coenzyme Q_{10}, it is preferable to be careful so that reduced coenzyme Q_{10} is not decomposed (e.g. so that reduced coenzyme Q_{10} is not oxidized to oxidized coenzyme Q_{10}). For that, the above-mentioned extraction (including cell disruption) is preferably carried out under an acidic to a weakly basic condition, and more preferably under an acidic to a neutral condition. In the case where a pH is used as an index, although it depends on the contact time, the pH is generally not more than 10, preferably not more than 9, more preferably not more than 8, and still more preferably not more than 7.

By the above-mentioned conditions, an oxidation reaction can be substantially prevented and, optionally, more strictly, the above-mentioned cell disruption and/or extraction are preferably carried out under the condition that reduced coenzyme Q_{10} is protected from an oxidation reaction. It is preferable to carry out at least the extraction under this condition, and it is more preferable to carry out the disruption and the extraction under this condition.

As "the condition that reduced coenzyme Q_{10} is protected from an oxidation reaction" means, for example, a deoxygenized atmosphere (an atmosphere of an inert gas such as nitrogen gas, carbon dioxide gas, helium gas, argon gas or hydrogen gas, reduced pressure, a boiling condition); a high salt concentration condition, for example, preferably a condition where salts (e.g. inorganic salts such as sodium chloride and sodium sulfate) are contained in not less than about 5% in an aqueous phase; the condition in the presence of a strong acid (e.g. an acid with a pKa value of not more than 2.5 in an aqueous solution), for example, in the presence of not less than 0.1 mole % of the strong acid relative to 1 mole of reduced coenzyme Q_{10}; and the condition in the presence of an antioxidant, for example, in the concomitant presence of ascorbic acid, citric acid, salts and esters thereof (e.g. not less than 0.1% by weight of them relative to reduced coenzyme Q_{10}). There may also be mentioned a reduction condition (a condition in which oxidized coenzyme Q_{10} can be converted into reduced coenzyme Q_{10}), for example, a condition involving a contact with a reducing agent such as dithionous acid.

By the above-mentioned culture (fermentation) and extraction, reduced coenzyme Q_{10} can be suitably produced and recovered. Preferably, an extract containing not less than 70 mole %, preferably not less than 75 mole % of reduced coenzyme Q_{10} among the entire coenzymes Q_{10} is obtained.

Thus-obtained extract containing reduced coenzyme Q_{10} is optionally purified by column chromatography, reduction treatment, or the like and then subjected to crystallization to obtain high-purity reduced coenzyme Q_{10} crystals. Incidentally, also in this case, a series of treatment steps are preferably carried out under "the condition that reduced coenzyme Q_{10} is protected from an oxidation reaction" mentioned above.

In the present invention, oxidized coenzyme Q_{10} can be produced by oxidizing the above-mentioned microbial cells or disrupted product thereof and then extracting oxidized coenzyme Q_{10} by an organic solvent, or extracting reduced coenzyme Q_{10} from the microbial cells or disrupted product thereof by an organic solvent, purifying optionally and oxidizing the resultant to oxidized coenzyme Q_{10}.

The above-mentioned oxidation may be carried out by, for example, mixing reduced coenzyme Q_{10} (preferably an aqueous suspension of the microbial cells or disrupted product thereof containing reduced coenzyme Q_{10}, an extract containing reduced coenzyme Q_{10} or the like) with an oxidizing agent (e.g. manganese dioxide or the like) and then, for example, oxidizing the mixture at room temperature (e.g. 30° C.) for not less than 30 minutes. In the case where the microbial cells or disrupted product thereof are oxidized, the extraction operation of oxidized coenzyme Q_{10} can be carried out in the same manner as the above-mentioned extraction operation of reduced coenzyme Q_{10}. Thereby, oxidized coenzyme Q_{10} can be efficiently recovered. Incidentally, it is not necessary to carry out the recovery of oxidized coenzyme Q_{10} under "the condition that reduced coenzyme Q_{10} is protected from an oxidation reaction", which is recommended for the recovery of reduced coenzyme Q_{10} and the recovery may be carried out in consideration of general safe operation and the like. The thus-obtained oxidized coenzyme Q_{10} may be optionally purified by column chromatography or the like, and, finally by conducting crystallization operation, high-purity oxidized coenzyme Q_{10} crystals may be obtained.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** shows a schematic diagram of a countercurrent 3-step continuous extraction apparatus used in Example 8.

BEST MODE FOR CARRYING OUT THE INVENTION

The following examples illustrate the present invention in further detail. These examples are, however, by no means limitative of the scope of the present invention.

Example 1

Various coenzyme Q_{10}-producing microorganisms shown in the following Tables 1 to 3 were cultured with shaking (amplitude: 2 cm, 310 reciprocation/min) at 25° C. for 72 hours in 10 mL of culture media [(glucose: 20 g, peptone: 5 g, yeast extract: 3 g, malt extract: 3 g)/L, pH: 6.0] using test tubes (inner diameter: 21 mm, entire length: 200 mm), and the obtained broth were optionally concentrated. Under a nitrogen atmosphere, in the concomitant presence of 3 parts by volume of isopropanol and 18.5 parts by volume of n-hexane relative to 10 parts by volume of the broth, the obtained solutions were vigorously shaken for 3 minutes using 10 parts by volume of glass beads (425 to 600 μm) to carry out cell disruption and extraction. The obtained hexane phases were evaporated (at 40° C.) under reduced pressure and analyzed by high performance liquid chromatography (HPLC) to determine the ratio and the production amount of reduced coenzyme Q_{10}.

HPLC conditions

Column: YMC-Pack 4.6×250 mm (manufactured by YMC. Co., Ltd.)

Mobile phase: methanol/n-hexane=85/15

Flow rate: 1 mL/min

Detection: UV 275 nm

The results are shown in Tables 1 to 3. The ratio of reduced coenzyme Q_{10} means a mole percentage value of the ratio of reduced coenzyme Q_{10} relative to the total of oxidized coenzyme Q_{10} and reduced coenzyme Q_{10} on the basis of the areas of the peaks of reduced coenzyme Q_{10} and oxidized coenzyme Q_{10} and the ratio of the mole absorption coefficients thereof (1:7.5).

TABLE 1

Strain name	Upper stand: Ratio of reduced coenzyme Q10 (%) Lower stand: Production amount of reduced coenzyme Q10 (μg/ml)
Agrobacterium tumefacience IFO 13263	82 7
Agrobacterium radiobacter ATCC 4718	78 7
Aspergillus clavatus JCM 1718	83 2
Acetobacter xylinum IFO15237	77 2
Aminobacter aganouensis JCM 7854	70 3
Agromonas oligotrophica JCM 1494	75 2
Acidiphilium multivorum JCM 8867	73 3
Bulleromyces albus IFO 1192	72 2
Bullera armeniaca IFO 10112	85 7
Brevundimonas diminuta JCM 2788	82 5
Cryptococcus laurentii IFO 0609	79 6
Chionosphaera apobasidialis CBS 7430	71 2
Candida curvata ATCC 10567	74 3
Cerinosterus luteoalbus JCM 2923	79 5
Exisophiala alcalophila JCM12519	77 3
Exobasidium gracile IFO7788	79 2
Fellomyces fuzhouensis IFO 10374	70 2
Filobasidiella neoformans CBS 132	88 2
Filobasidium capsuloigenum CBS 1906	82 3
Geotrichum capitatum JCM 6258	77 3
Graphiola cylindrica IFO 6426	75 4
Gluconobacter suboxydans IFO 3257	86 6
Kockovaella imperatae JCM 7826	78 2

TABLE 2

Strain name	Upper stand: Ratio of reduced coenzyme Q10 (%) Lower stand: Production amount of reduced coenzyme Q10 (μg/ml)
Kurtzmanomyces nectairei IFO 10118	79 2

TABLE 2-continued

Strain name	Upper stand: Ratio of reduced coenzyme Q10 (%) Lower stand: Production amount of reduced coenzyme Q10 (μg/ml)
Lalaria cerasi CBS 275.28	75
	2
Leucosporidium scottii IFO 1212	88
	6
Legionella anisa JCM 7573	73
	3
Methylobacterium extorguens JCM 2802	72
	2
Mycoplana ramosa JCM 7822	80
	2
Oosporidium margaritiferum CBS2531	76
	2
Pseudomonas denitrificans IAM 12023	85
	8
Pseudomonas shuylkilliensis IAM 1092	84
	6
Psedozyma aphidis CBS 517.23	79
	5
Paracoccus denitrificans JCM 6892	83
	5
Petromyces alliaceus IFO 7538	72
	2
Rhodotorula glutinis IFO 1125	79
	7
Rhodotorula minuta IFO 0387	74
	8
Rhodosporidium diobovatum ATCC 1830	86
	4
Rhizomonas suberifaciens IFO 15212	82
	2
Rhodobium orients JCM 9337	80
	2
Rhodoplanes elegans JCM9224	74
	2
Rhodopseudomonas palustris JCM2524	90
	6
Rhodobacter capsulatus SB 1003	95
	6
Sporobolomyces holsaticus IFO 1034	72
	9
Sporobolomyces pararoseus IFO 0471	93
	8
Sporidiobolus johnsonii IFO 1840	73
	7
Saitoella complicata IFO 10748	97
	9

TABLE 3

Strain name	Upper stand: Ratio of reduced coenzyme Q10 (%) Lower stand: Production amount of reduced coenzyme Q10 (μg/ml)
Schizosaccharomyces pombe IFO 0347	90
	8
Sphingomonas parapaucimobilis IFO 15100	78
	7
Sporotrichum cellulophilium ATCC 20493	73
	6
Sympodiomycopsis paphiopedili JCM 8318	80
	6
Sterigmatosporidium polymorphum IFO 10121	72
	2
Sphingomonas adhesiva JCM 7370	80
	3

TABLE 3-continued

Strain name	Upper stand: Ratio of reduced coenzyme Q10 (%) Lower stand: Production amount of reduced coenzyme Q10 (μg/ml)
Tapharina caerulescens CBS 351.35	81
	2
Tremella mesenterica ATCC 24438	89
	3
Trichosporon cutaneum IFO 1198	95
	8
Tilletiaria anomala CBS 436.72	75
	4
Tilletia caries JCM 1761	80
	3
Tolyposporium bullatum JCM 2006	73
	4
Tilletiopsis washintonesis CBS 544	76
	2
Ustilago esculenta IFO 9887	78
	2
Udeniomyces megalosporus JCM 5269	87
	2
Xanthophilomyces dendrorhous IFO 10129	84
	2
Xanthobacter flavus JCM1204	80
	2
Paecilomyces lilacinus ATCC10114	80
	5
Acremonium chrysogenum ATCC11550	75
	5
Hyphomonas hirschiana ATCC33886	72
	3
Rhizobium meliloti ATCC9930	85
	10

Example 2

Rhodotorula glutinis IFO1125 was aerobically cultured at 25° C. for 48 hours in a culture medium (peptone: 5 g, yeast extract: 3 g, malt extract: 3 g, glucose: 20 g/L, pH: 6.0). The cells after the culture were collected by centrifugation and suspended in a phosphoric acid buffer solution at pH 7 to which N-methyl-N'-nitro-N-nitrosoguanidine have been added so as to have its concentration of 200 μg/mL. After maintaining the solution at 25° C. for 1 hour, the cells were washed for 5 times with a 0.9% NaCl solution and further suspended in a 0.9% NaCl solution. The obtained cell suspension was properly diluted and a colony was to be formed on an agar plate of the above-mentioned culture medium. The production amount and the ratio of reduced coenzyme Q_{10} in the isolated mutant strain were determined in the same manner as Example 1. The strains having higher production amount and the ratio of reduced coenzyme Q_{10} as compared with those of wild strains was further mutated repeatedly. As the result, by repeating the mutagenesis for 10 times, mutant strains with productivity of not less than 15 μg/mL were obtained. In this case, the ratio of reduced coenzyme Q_{10} was not less than 80 mole %.

Example 3

Saitoella complicata IFO 10748 was aerobically cultured at 25° C. for 72 hours in 10 L of a culture medium (peptone: 5 g, yeast extract: 3 g, malt extract: 3 g, glucose: 20 g/L, pH: 6.0). The obtained cells were disrupted for 2 times at 80 MPa of disruption pressure by a pressure homogenizer (manufactured by Lanni Co.) sealed with nitrogen gas to obtain a

cell-disrupted solution. The cell-disrupted solution was subjected to extraction with 30 parts by volume of isopropanol and 40 parts by volume of hexane for 3 times to obtain an extract. The extraction ratio was 99%. The ratio of reduced coenzyme Q_{10} was 97 mole W.

Example 4

When mutant strains of *Rhodotorula glutinis* IFO1125 were aerobically cultured at 25° C. in 10 L of a culture medium (peptone: 10 g, yeast extract: 5 g, malt extract: 3 g, glucose: 20 g/L, pH: 6.0), glucose was fed at the rate of 4 g/h after the lapse of 48 hours to 96 hours (fed glucose amount: 190 g). The production amount of reduced coenzyme Q_{10} per culture medium was not less than 20 μg/mL and the ratio of reduced coenzyme Q_{10} was not less than 80 mole %.

Example 5

The extract obtained in Example 3 was subjected to solvent substitution with a hexane solution, the resultant was adsorbed in a column filled with silica gel and subjected to development and elution by a solution of n-hexane/diethyl ether (9/1) to obtain a fraction containing reduced coenzyme Q_{10}. Furthermore, the fraction was cooled to 2° C. with stirring to obtain a white slurry. All the above-mentioned operations were carried out in a nitrogen atmosphere. The obtained slurry was filtered under reduced pressure, the resulting wet crystals were washed with the development solution same as used above (the temperature of the solvent used for washing was 2° C.), and the wet crystals were dried under reduced pressure (20 to 40° C., 1 to 30 mmHg) to obtain 81 mg of white dry crystals. The purity of the obtained crystals was 99.9% and the ratio of reduced coenzyme Q_{10} was 90 mole %.

Example 6

The extract obtained in Example 3 was subjected to solvent substitution with n-hexane, the resultant was added with 50 mg of manganese dioxide, and the mixture was stirred at 30° C. for 30 minutes. Thus-obtained reaction solution was fractionated and purified in the same manner as Example 5 to obtain 74 mg of high-purity oxidized coenzyme Q_{10}.

Example 7

Saitoella complicata IFO 10748 was aerobically cultured at 25° C. for 72 hours in 500 mL of a culture medium (peptone: 5 g, yeast extract: 3 g, malt extract: 3 g, glucose: 20 g/L, pH: 6.0). The obtained cells were disrupted for 2 times at 80 MPa of disruption pressure by a pressure homogenizer (manufactured by Lanni Co.) sealed with nitrogen gas to obtain a cell-disrupted solution. The ratio of reduced coenzyme Q_{10} in the cell-disrupted solution was 97% relative to the entire coenzymes Q_{10} including oxidized coenzyme Q_{10}. 200 mL of the cell-disrupted solution was mixed with isopropanol and n-hexane at the ratios shown in the first extraction section in the following Table 4 so as to adjust the total solvent amount to be 500 mL and the mixtures were stirred at 40° C. for 30 minutes to carry out the first extraction. After completion of the extraction, the resultants were kept standing for 10 minutes and the separated upper layers were collected. The volume ratios of the lower layers (residues) relative to the total solution amounts were defined as indexes of separability and shown as the interface positions in Table 4.

Furthermore, in order to carry out the second extraction, the solvent concentrations of the residual layers were measured and isopropanol and hexane were further added so as to keep the solvent ratios in the entire solutions be the ratios shown in the second extraction section in Table 4. The resulting solutions were stirred at 40° C. for 30 minutes. Then, the solutions were kept standing for 10 minutes and the upper layers were collected in the same manner as described above to determine the solvent concentrations of the residual layers. Isopropanol and hexane were added thereto so as to keep the solvent ratios in the entire solutions be the ratios shown in the third extraction section in Table 4, and the solutions were stirred at 25° C. for 30 minutes to carry out the third extraction.

The ratios of the amounts of reduced coenzyme Q_{10} contained in the collected upper layers of each of the first, second and third steps relative to the amount of reduced coenzyme Q_{10} contained in the cell-disrupted solution or the extraction residue before the extraction were defined as the extraction ratios of reduced coenzyme Q_{10} in the respective steps. The calculation results are shown in Table 4. The integrated extraction ratios of reduced coenzyme Q_{10} in the second and third extraction steps are also shown. In any steps, the static separability was excellent and the integrated extraction ratio in the case where extraction was repeated for 3 times was as high as not less than 90% to show high recovery ratio. Particularly, in the case where the isopropanol concentration was adjusted to be not less than 30%, the recovery ratio was as high as not less than 99%.

TABLE 4

		Solvent ratio (vol %)		Interface	Extraction ratio (%)	
		Isopropanol	Hexane	position	Respective extraction ratio	Integrated extraction ratio
Case1	First	18.8	52.7	0.492	73.6	73.6
	Second	19.0	52.4	0.624	47.6	86.2
	Third	29.7	41.7	0.645	55.5	93.8
Case2	First	31.3	40.2	0.499	90.7	90.7
	Second	37.7	33.7	0.549	83.7	98.5
	Third	40.6	30.9	0.565	40.1	99.1
Case3	First	31.3	40.2	0.526	89.0	89.0
	Second	34.1	37.3	0.553	85.8	98.3
	Third	36.8	34.6	0.555	46.6	99.1
Case4	First	31.3	40.2	0.526	89.0	89.0
	Second	34.1	37.3	0.553	85.8	98.3
	Third	42.4	29.0	0.644	50.0	99.0

TABLE 4-continued

		Solvent ratio (vol %)		Interface	Extraction ratio (%) Respective extraction	Integrated extraction
		Isopropanol	Hexane	position	ratio	ratio
Case5	First	31.3	40.2	0.526	89.0	89.0
	Second	40.1	31.4	0.595	88.1	98.6
	Third	40.7	30.7	0.593	45.3	99.1
Case6	First	31.3	40.2	0.526	89.0	89.0
	Second	40.1	31.4	0.595	88.1	98.6
	Third	45.8	25.7	0.663	40.7	99.0

Example 8

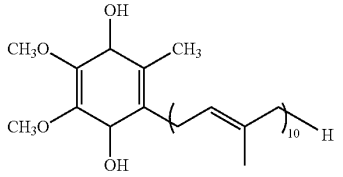
Saitoella complicata IFO 10748 was aerobically cultured at 25° C. for 72 hours in 750 L of a culture medium (peptone: 5 g, yeast extract: 3 g, malt extract: 3 g, glucose: 20 g/L, pH: 6.0). The obtained cells were disrupted for 2 times at 140 MPa of disruption pressure by a pressure homogenizer (manufactured by Lanni Co.) sealed with nitrogen gas to obtain a cell-disrupted solution. The cell-disrupted solution was subjected to continuous extraction by a countercurrent 3-step continuous extraction apparatus shown in FIG. **1**. The capacity of the stirring tank was 630 L and the capacity of the static separation tank was 200 L. The cell-disrupted solution was supplied to the first stirring tank and isopropanol and n-hexane were supplied to respective steps. The supply amount of the cell-disrupted solution was 2 L/min and the supply amounts of isopropanol and n-hexane were adjusted to be 1.3 L/min for isopropanol and 3.7 L/min for n-hexane as the total of the supply amounts in respective steps. In this case, the solvent concentration in respective steps was properly adjusted so that the isopropanol concentration of 5 to 50 v/v % and the n-hexane concentration of 25 to 65 v/v % were kept. The extraction temperature was 40° C. and the treatment duration was 6 hours. At the point after the lapse of 6 hours, the recovery ratio of reduced coenzyme Q_{10} extracted from the cell-disrupted solution was calculated on the basis of reduced coenzyme Q_{10} remaining in the extraction residue in the static separation tank in the third step to find the recovery ratio of 98.9%. The static separation was well carried out during the entire operation period and stable continuous extraction was possible.

INDUSTRIAL APPLICABILITY

According to the processes of the present invention, reduced coenzyme Q_{10} can be produced cheaply on the industrial scale by considerably simple steps comprising culturing microorganisms and recovering reduced coenzyme Q_{10}. In addition, oxidized coenzyme Q_{10} can also be produced by simple processes.

The invention claimed is:

1. A process for producing on an industrial scale the oxidized coenzyme Q_{10} represented by the following formula:



which comprises culturing reduced coenzyme Q_{10}-producing microorganisms in a culture medium containing a carbon source, a nitrogen source, a phosphorus source and a micronutrient to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10},

disrupting the microbial cells to obtain reduced coenzyme Q_{10}; and

oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10} and then extracting the oxidized coenzyme Q_{10} by an organic solvent under an inert gas atmosphere.

2. The process according to claim **1**,

wherein the extraction of the oxidized coenzyme Q_{10} is carried out by using a hydrophilic organic solvent.

3. The process according to claim **1**,

wherein the extraction of the oxidized coenzyme Q_{10} is carried out by using a hydrophobic organic solvent.

4. The process according to claim **1**, wherein the reduced coenzyme Q_{10} is oxidized with an oxidizing agent.

5. The process according to claim **4**, wherein the oxidizing agent is manganese dioxide.

6. The process according to claim **1**, wherein the oxidized coenzyme Q_{10} is extracted by a continuous extraction.

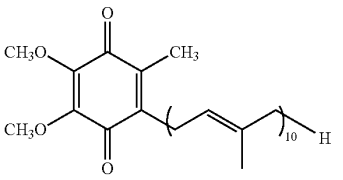
7. The process according to claim **6**, wherein the continuous extraction is a countercurrent multistage extraction.

8. The process according to claim **1**, wherein the reduced coenzyme Q_{10} upon disrupting has a ratio of not less than 70 mole % among the entire coenzymes Q_{10} when measured under the condition that the reduced coenzyme Q_{10} is protected from an oxidation reaction.

9. The process according to claim **1**, wherein the inert gas atmosphere comprises nitrogen gas.

10. The process according to claim **1**, wherein the culture medium is at least 750 L.

11. A process for producing on an industrial scale the oxidized coenzyme Q_{10} represented by the following formula:



which comprises culturing reduced coenzyme Q_{10}-producing microorganisms in a culture medium containing a carbon source, a nitrogen source, a phosphorus source and a micronutrient to obtain microbial cells containing

reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10},

extracting the reduced coenzyme Q_{10} by an organic solvent under an inert gas atmosphere, and

oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}.

12. The process according to claim **11**,

wherein the extraction of the reduced coenzyme Q_{10} is carried out by using a hydrophilic organic solvent.

13. The process according to claim **11**,

wherein the extraction of the reduced coenzyme Q_{10} is carried out by using a hydrophobic organic solvent.

14. The process according to claim **11**, further comprising the step of disrupting the microbial cells.

15. The process according to claim **11**, wherein the reduced coenzyme Q_{10} is oxidized with an oxidizing agent.

16. The process according to claim **15**, wherein the oxidizing agent is manganese dioxide.

17. The process according to claim **11**, wherein the reduced coenzyme Q_{10} is extracted by a continuous extraction.

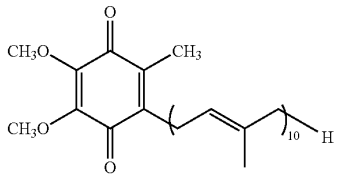
18. The process according to claim **17**, wherein the continuous extraction is a countercurrent multistage extraction.

19. The process according to claim **11**, wherein the reduced coenzyme Q_{10} upon extracting has a ratio of not less than 70 mole % among the entire coenzymes Q_{10} when measured under the condition that the reduced coenzyme Q_{10} is protected from an oxidation reaction.

20. The process according to claim **11**, wherein the inert gas atmosphere comprises nitrogen gas.

21. The process according to claim **11**, wherein the culture medium is at least 750 L.

22. A process for producing on an industrial scale the oxidized coenzyme Q_{10} represented by the following formula:



which comprises culturing reduced coenzyme Q_{10}-producing microorganisms in a culture medium containing a carbon source, a nitrogen source, a phosphorus source and a micronutrient to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10},

disrupting the microbial cells to obtain reduced coenzyme Q_{10}; and

oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10} and then extracting the oxidized coenzyme Q_{10} by an organic solvent in a sealed tank.

23. The process according to claim **22**,

wherein the extraction of the oxidized coenzyme Q_{10} is carried out by using a hydrophilic organic solvent.

24. The process according to claim **22**,

wherein the extraction of the oxidized coenzyme Q_{10} is carried out by using a hydrophobic organic solvent.

25. The process according to claim **22**, wherein the reduced coenzyme Q_{10} is oxidized with an oxidizing agent.

26. The process according to claim **25**, wherein the oxidizing agent is manganese dioxide.

27. The process according to claim **22**, wherein the oxidized coenzyme Q_{10} is extracted by a continuous extraction.

28. The process according to claim **27**, wherein the continuous extraction is a countercurrent multistage extraction.

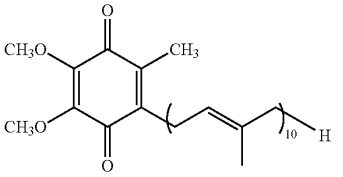
29. The process according to claim **22**, wherein the sealed tank is sealed under an inert gas atmosphere.

30. The process according to claim **29**, wherein the inert gas atmosphere comprises nitrogen gas.

31. The process according to claim **22**, wherein the culture medium is at least 750 L.

32. The process according to claim **22**, wherein the reduced coenzyme Q_{10} upon disrupting has a ratio of not less than 70 mole % among the entire coenzymes Q_{10} when measured under the condition that the reduced coenzyme Q_{10} is protected from an oxidation reaction.

33. A process for producing on an industrial scale the oxidized coenzyme Q_{10} represented by the following formula:



which comprises culturing reduced coenzyme Q_{10}-producing microorganisms in a culture medium containing a carbon source, a nitrogen source, a phosphorus source and a micronutrient to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10},

extracting the reduced coenzyme Q_{10} by an organic solvent in a sealed tank, and

oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}.

34. The process according to claim **33**,

wherein the extraction of reduced coenzyme Q_{10} is carried out by using a hydrophilic organic solvent.

35. The process according to claim **33**,

wherein the extraction of the reduced coenzyme Q_{10} is carried out by using a hydrophobic organic solvent.

36. The process according to claim **33**, further comprising disrupting the microbial cells.

37. The process according to claim **33**, wherein the reduced coenzyme Q_{10} is oxidized with an oxidizing agent.

38. The process according to claim **37**, wherein the oxidizing agent is manganese dioxide.

39. The process according to claim **33**, wherein the reduced coenzyme Q_{10} is extracted by a continuous extraction.

40. The process according to claim **39**, wherein the continuous extraction is a countercurrent multistage extraction.

41. The process according to claim **33**, wherein the sealed tank is sealed under a deoxygenized atmosphere.

42. The process according to claim **41**, wherein the deoxygenized atmosphere comprises inert gas.

43. The process according to claim **41**, wherein the deoxygenized atmosphere comprises nitrogen gas.

44. The process according to claim **33**, wherein the culture medium is at least 750 L.

45. The process according to claim **33**, wherein the reduced coenzyme Q_{10} upon extracting has a ratio of not less than 70 mole % among the entire coenzymes Q_{10} when measured under the condition that the reduced coenzyme Q_{10} is protected from an oxidation reaction.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

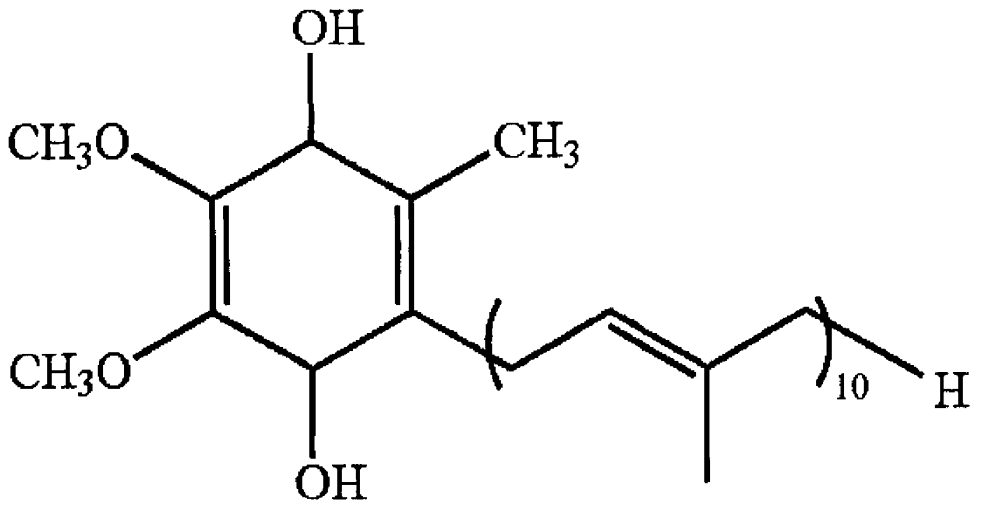
CERTIFICATE OF CORRECTION

PATENT NO. : 7,910,340 B2
APPLICATION NO. : 11/981181
DATED : March 22, 2011
INVENTOR(S) : Kazuyoshi Yajima et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In column 1, line 6;
Change "si" to --is--

In claim 1, column 23, lines 57-65
Change



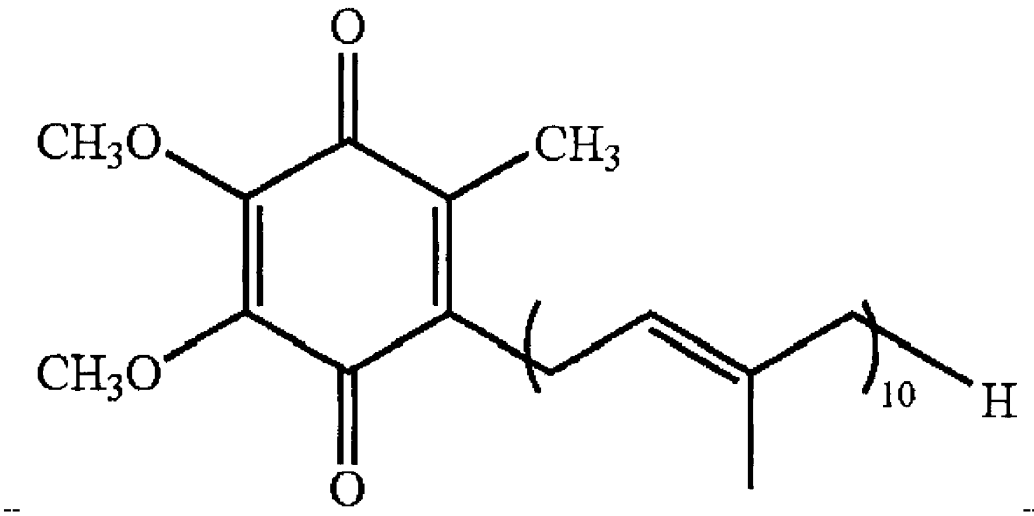
"

to

Signed and Sealed this
Thirty-first Day of May, 2011

David J. Kappos

David J. Kappos
Director of the United States Patent and Trademark Office


O
CH3O
CH3
CH3O
10
H
O

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA
WESTERN DIVISION

KANEKA CORPORATION,

Plaintiff,

v.

XIAMEN KINGDOMWAY GROUP CO., PACIFIC RAINBOW INTERNATIONAL INC., MITSUBISHI GAS CHEMICAL COMPANY, INC., MAYPRO INDUSTRIES, INC., and SHENZHOU BIOLOGY & TECHNOLOGY CO., LTD.,

Defendants.

Case No. 2:11-cv-02389-MRP

Claim Construction Order

I. Introduction

Plaintiff Kaneka Corporation ("Plaintiff") has asserted U.S. Patent No. 7,910,340 (the '340 Patent) against defendants Xiamen Kingdomway Group Co., Pacific Rainbow International Inc., Maypro Industries, Inc., and Shenzhou Biology & Technology Co., Ltd. (collectively "Defendants"). The '340 Patent relates to processes for producing the chemical coenzyme Q_{10} (CoQ_{10}) on an industrial scale.

In this Order, the Court construes the following claim terms: (1) "inert gas atmosphere," (2) "sealed tank," (3) "culturing reduced coenzyme Q_{10} producing microorganisms . . . to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10}," and (4) related terms "oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" and "oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}."

The '340 Patent has been the subject of several lawsuits. Plaintiff filed its complaint for patent infringement in this Court on March 22, 2011. Complaint (Docket No. 1). On the same day, ZMC-USA, L.L.C. ("ZMC"), filed for declaratory relief against Plaintiff regarding the '340 Patent in the Eastern District of Texas ("the Texas Litigation"), and the Court subsequently transferred Plaintiff's claims against defendants ZMC and Zhejiang Medicine Co., Ltd. to Texas. Order re Transfer (Docket No. 39); Order Severing and Transferring Claims to the United States District Court for the Southern District of Texas (Docket No. 47). On June 17, 2011, Plaintiff filed a complaint in the International Trade Commission. *See* Certain Coenzyme Q10 Products and Methods of Making Same, Inv. No. 333-TA-790, USITC Pub. 4407 (September 27, 2012) (Final) ("the ITC Proceeding"); *see also* Stipulation To Stay District Court Action Pending ITC Investigation (Docket No. 58) at 1. The Court granted the parties' motion to stay this case. Order re Stipulation to Stay District Court Action Pending ITC Investigation (Docket No. 59). The stay was lifted on February 7, 2013 after the conclusion of the ITC Proceeding. Status Report – Joint (Docket No. 70). Claim construction orders have been issued in both the ITC Proceeding and the Texas Litigation.

II. Principles of Claim Construction

The purpose of claim construction is to determine the meaning and scope of the patent claims alleged to be infringed. *O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1360 (Fed. Cir. 2008). Claim construction is a pure

question of law. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 384, 391 (1996). For purposes of claim construction, the Court reviews both intrinsic and extrinsic evidence, placing emphasis on the former.

A. Intrinsic Evidence

i. Claim Language

"The words of a claim 'are generally given their ordinary and customary meaning.'" *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (citation omitted). "[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Id.* at 1313. "The inquiry into how a person of ordinary skill in the art understands a claim term provides an objective baseline from which to begin claim interpretation." *Id.* "That starting point is based on the well-settled understanding that inventors are typically persons skilled in the field of the invention and that patents are addressed to and intended to be read by others of skill in the pertinent art." *Id.*

ii. Specification

The specification is "always highly relevant to the claim construction analysis." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 978 (Fed. Cir. 1995). As Judge Rich wrote shortly after the creation of the Federal Circuit, "the specification . . . is the primary basis for construing the claims." *Standard Oil Co. v. Am. Cyanamid Co.*, 774 F.2d 448, 452 (Fed. Cir. 1985). "[T]he specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Phillips*, 415 F.3d at 1316. "In other cases, the specification may reveal an intentional disclaimer, or disavowal, of claim scope by the inventor." *Id*. In such

//

//

cases, the inventor's intention as expressed in the specification "is regarded as dispositive." *Id.*

iii. Prosecution History

The Court also considers the patent's prosecution history. "The prosecution history, which we have designated as part of the 'intrinsic evidence,' consists of the complete record of the proceedings before the PTO and includes the prior art cited during the examination of the patent." *Id*. The patentee created the prosecution history by explaining its invention and claims to the PTO in order to obtain the patent, and thus the prosecution history provides evidence about how the PTO and the inventor understood the patent. *Id*. "Yet because the prosecution history represents an ongoing negotiation between the PTO and the applicant, rather than the final product of that negotiation, it often lacks the clarity of the specification and thus is less useful for claim construction purposes." *Id*. "Nonetheless, the prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Id*.

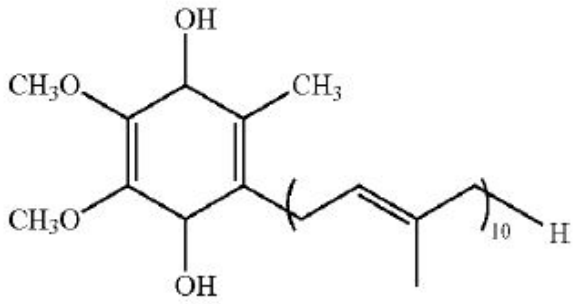
B. Extrinsic Evidence

In addition to using intrinsic evidence, this Court is also authorized to use extrinsic evidence in claim construction. *Phillips*, 415 F.3d at 1317 ("[W]e have . . . authorized district courts to rely on extrinsic evidence . . . ."). Extrinsic evidence "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Id*. While extrinsic evidence can shed light on claim meaning, it is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" *Id*. (citation omitted). Finally, extrinsic evidence is "unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." *Id.* at 1319.

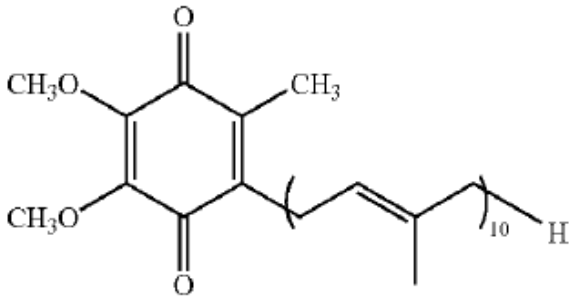
III. Technical Background

Plaintiff asserts claims 1, 8-9, 11, 19-20, 22, 30, 32-33, 43, and 45 of the '340 Patent. The asserted claims are directed to processes for producing oxidized CoQ_{10} on an industrial scale.

CoQ_{10} is biosynthesized naturally in the membranes of animal cells where it is used to produce adenosine triphosphate to aid in cellular respiration. The '340 Patent at 1:61-65; *see also* Kaneka's Brief on Claim Construction under *Markman* (Docket No. 132) at 2. CoQ_{10} exists in three forms: oxidized, semi-oxidized, and reduced. In cells, CoQ_{10} undergoes redox reactions, causing electron transfer and changing the form of the CoQ_{10}. The claims of the '340 Patent are directed to processes by which the reduced form of CoQ_{10} is produced at a provided mole percentage and the reduced CoQ_{10} is oxidized. Reduced CoQ_{10} is represented by the molecular formula $C_{59}H_{92}O_4$ and the following molecular structure:



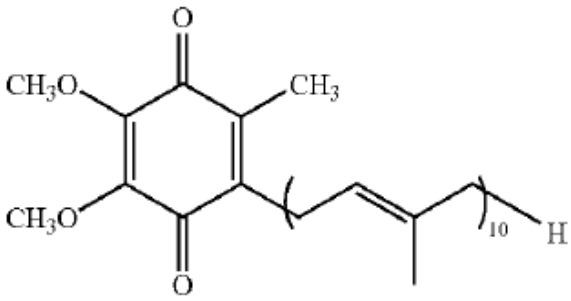
The '340 Patent at 1:20-27. Oxidized CoQ_{10} is represented by the molecular formula $C_{59}H_{90}O_4$ and the following molecular structure:



Id. at 1:33-40.

Claim 11 provides an example of the asserted independent claims and reads as follows:

> 11. A process for producing on an industrial scale the oxidized coenzyme Q_{10} represented by the following formula:



> which comprises ***culturing reduced coenzyme Q_{10}-producing microorganisms*** in a culture medium containing a carbon source, a nitrogen source, a phosphorus source and a micronutrient ***to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10}***,
>
> extracting the reduced coenzyme Q_{10} by an organic solvent under an ***inert gas atmosphere***, and
>
> ***oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}***.

The '340 Patent at 24:50-25:6. Independent claim 1 provides an additional disrupting step, and describes the oxidizing and extracting steps as follows:

> ***oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10} and then extracting the oxidized coenzyme Q_{10}*** by an organic solvent under an inert gas atmosphere.

Id. at 23:56-24:25. Independent claims 22 and 33 differ from claims 1 and 11 respectively in that they require that the extracting step occur "in a ***sealed tank***" rather than under an inert gas atmosphere. *Id*. at 25:32-54, 26:13-36.

//

IV. Claim Construction

A. "inert gas atmosphere"

Claim Nos.	Claim Term	Plaintiff's Construction	Defendants' Construction
1, 11	**"inert gas atmosphere"**	"a gas atmosphere that is less readily reactive with the organic solvent"	"an atmosphere of inert gas (such as nitrogen, carbon dioxide, helium, argon, or hydrogen) that is free or substantially free of oxygen"

Plaintiff argues that the inert gas atmosphere may include reactive gases. The independent claims use the term "comprising," which is a patent term of art denoting an open-ended claim. In addition, the specification states that "complete oxygen elimination is very difficult to achieve." The '340 Patent at 10:60-61. According to Plaintiff, this evidence shows that an inert gas atmosphere cannot be interpreted to mean an atmosphere free of oxygen.[1] Instead, the term must be construed in light of safety concerns regarding reactivity.

Defendants argue that an inert gas atmosphere is an atmosphere free of reactive, oxidizing gases. The term "inert gas" appears once in the specification, as an example of a deoxygenized atmosphere:

> As "the condition that reduced coenzyme Q_{10} is protected from an oxidation reaction" means, for example, a deoxygenized atmosphere (an atmosphere of an inert gas such as nitrogen gas, carbon dioxide gas, helium gas, argon gas or hydrogen gas, reduced pressure, a boiling condition); a high salt concentration condition . . . ; the

[1] The Court also notes that Plaintiff presented dependent claims 8 and 19 to argue for claim differentiation. Plaintiff states, "In dependent claims 8 and 19, the inventors claimed one type of an 'inert gas atmosphere' which is 'protected from an oxidation reaction' (a 'deoxygenized atmosphere'). Plaintiff's Brief at 13. Claims 8 and 19 in no way modify the term "inert gas atmosphere" and instead describe a separate condition for measuring the mole percent of the reduced CoQ_{10}. It would therefore be impossible for any interpretation of "inert gas atmosphere" to render dependent claims 8 and 19 "superfluous" as Plaintiff claims. The Court will therefore not consider this argument.

> condition in the presence of a strong acid . . . ; and the condition in the presence of an antioxidant.

The '340 Patent at 16:35-48. Defendants also present expert testimony from the ITC Proceeding stating that a person of ordinary skill in the art would understand an inert gas atmosphere to be an atmosphere free or substantially free of oxygen. Defendant's Opening Claim Construction Brief (Docket No. 139) at Ex. 8, A134-35 at 36-37, Ex. 10 at A4-1 to A4-2.

Plaintiff presented the same argument in the ITC Proceeding and the Texas Litigation. ITC Proceeding at 32-37; Order at 36-41, *Zhejiang Med. Co. v. Kaneka Corp.*, No. H-11-1052 (S.D. Tex. Aug. 23 2012) ("Texas Order"). The Court adopts the reasoning presented in both the ITC Proceeding and the Texas Order with respect to the claim construction of the term "under an inert gas atmosphere" in their entirety. *See* ITC Proceeding at 32-37; Texas Order at 36-41. Although these decisions have no binding precedential effect, the Court has drawn the same conclusions using the same intrinsic evidence and substantially the same extrinsic evidence presented in those cases.

To these thorough descriptions of the evidence, one additional point is in order. Plaintiff has acted as its own lexicographer in its specification by defining an environment for protecting against an oxidation reaction by examples including a deoxygenized atmosphere. The '340 Patent at 16:35-37. An "atmosphere of inert gas" is then offered as an example of such a deoxygenized atmosphere. *Id*. at 16:36-39. Plaintiff's construction requires that the definition of an "inert gas atmosphere" includes oxygenized atmospheres, which would contradict the definition and examples provided in the specification.

The Court finds that **"inert gas atmosphere"** means **"a gas atmosphere that is free or substantially free of oxygen and reactive gases."**

//

//

B. "sealed tank"

Claim Nos.	Claim Term	Plaintiff's Construction	Defendants' Construction
22, 33	**"sealed tank"**	"a tank that substantially prevents direct exposure of its contents to the atmosphere"	"a tank that is closed to prevent the entry or exit of materials"

Plaintiff argues that the term "sealed tank" should be construed with respect to safety considerations and Fig. 1 of the '340 Patent, which Plaintiff describes as "depict[ing] the flow of materials from one 'sealed tank' to another." Plaintiff's Brief at 17. Plaintiff states that its construction is consistent with the plain and ordinary meaning of the term as understood by a person of ordinary skill in the art at the time of invention. Defendants argue that the term "sealed" should be construed according to its plain and ordinary meaning and present extrinsic evidence including expert testimony from the ITC Proceeding and dictionary definitions.

Plaintiff presented the same argument in the ITC Proceeding. ITC Proceeding at 40-50. The Court adopts the reasoning presented in the ITC Proceeding with respect to the claim construction of the term "sealed tank" in its entirety. *See id*. The Court has again drawn the same conclusions using the same intrinsic evidence and substantially the same extrinsic evidence presented in that case.[2]

The Court finds that **"sealed tank"** means **"a tank that is closed to prevent the entry or exit of materials."**

[2] Plaintiff provided an expert report from an additional expert, Dr. Moriera, ("the Moriera Report") who did not appear before the ITC. Plaintiff prepared and served the Moriera Report on different parties in the Texas Litigation. The Moriera Report was not served on Defendants in this litigation, and Defendants have had no opportunity to cross-examine or rebut the Moriera Report. The procedural requirements for evidence provided by experts are important to ensure reliable application of "the principles and methods" of the scientific inquiry to "the facts of the case." FED. R. EVID. 702(d); *see also* FED. R. EVID. 703. Both Plaintiff and Defendants had the opportunity to cross-examine or rebut expert reports and testimony submitted in the ITC Proceeding. Consequently, the Court gives greater weight to the extrinsic evidence from the ITC Proceeding over the Moriera Report.

C. "culturing reduced coenzyme Q_{10} producing microorganisms . . . to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10}"

Claim Nos.	Claim Term	Plaintiff's Construction	Defendants' Construction
1, 11, 22, 33	**"culturing reduced coenzyme Q_{10} producing microorganisms . . . to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10}"**	No construction necessary. Alternatively: "culturing (i.e., growing of living cells in a controlled artificial environment) reduced coenzyme Q_{10} (i.e., class of 2,3-Dimethoxy-5-methyl quinones, semiquinones, and quinols with ten isoprene units substituted at the C-6 position), producing microorganisms to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10} (reduced coenzyme Q_{10} comprises ≥ 70 mole % of the total coenzyme Q_{10}, i.e., reduced coenzyme Q_{10} plus oxidized coenzyme Q_{10})"	"culturing reduced coenzyme Q_{10} producing microorganisms to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10} as determined by the assay described at col. 5, line 8 to line 43, and Example 1 of the '340 patent"

Plaintiff argues that no construction is necessary for the term "culturing reduced coenzyme Q_{10} producing microorganisms . . . to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10}" or, alternatively, that non-limiting examples from the specification

may be listed to sufficiently clarify the term. Defendants argue in support of adding a testing method for the mole percent, as described in an example provided in the specification of the '340 Patent. The primary disagreement between the parties appears to be over the timing and method for determining the mole percent of reduced CoQ_{10}. This aspect of the claim language has not been argued in either the ITC Proceeding and the Texas Litigation.

Generally, "particular embodiments and examples appearing in the specification will not [] be read into the claims." *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998) (quotation omitted). Indeed, it is well known that while a claim is construed in light of the specification, a Court must tread carefully to avoid "reading a limitation from the written description into the claims." *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1340-41 (Fed. Cir. 2001). Accordingly, any requirement as to the timing of the mole percent determination or the method of mole percent determination must be considered carefully and incorporated only if justified by the claim itself.

The claims do not explicitly state a timing requirement for the mole percent determination, but, due to the structure of the claims, there is an implicit limitation as to the timing requirement. The claims of the '340 Patent describe "culturing" CoQ_{10}-producing "microorganisms . . . to obtain microbial cells containing" a specific mole percent of reduced CoQ_{10}. Claims 1 and 22 refer to obtaining this "reduced" CoQ_{10} and oxidizing the "thus-obtained reduced" CoQ_{10}. Claims 11 and 33 refer to extracting "the reduced" CoQ_{10} and oxidizing "the extracted reduced" CoQ_{10}. Although steps in a method or process claim generally need not be performed in the same order listed in the claims, the language of the claims may require that steps be performed in a certain order. *See, e.g.*, *Interactive Gift Exp., Inc. v. Compuserve, Inc.*, 256 F.3d 1323, 1342 (Fed. Cir. 2001). The addition of these modifiers—"thus-obtained," "the reduced," and "the reduced oxidized"—requires that the steps be performed in the order listed. It would be impossible to

oxidize "thus-obtained" CoQ_{10} without first executing the step necessary to obtain it.

The mole percent term appears in the claim limitation addressing the reduced CoQ_{10} obtained from the microbial cells. Other steps, such as disruption, oxidation, and extraction, affect the mole percent of reduced CoQ_{10}. *See* Kaneka's Responsive Brief on Claim Construction Under *Markman* (Docket No. 141) at 7-9 (describing the aerobic culturing process). Since the steps must be performed in order, and the other steps of the claim affect the mole percent of reduced CoQ_{10}, the mole percent of reduced CoQ_{10} must be determined at a time prior to the execution of any of the subsequent steps of the claims. In addition, the claim limitation directed to the mole percent of the reduced CoQ_{10} appears with reference to the culturing step. Allowing the determination of the mole percent of reduced CoQ_{10} to occur at any point in the patented process would ignore the plain language of the claim.

The claims also do not explicitly state a specific method of testing to determine the mole percent of the reduced CoQ_{10}. It is, however, clear to the parties and the Court how critical the method of testing is to the determination of infringement. The ITC Proceeding details the difficulties resulting from using different storage and testing methods to determine the mole percent of reduced CoQ_{10}. *See* ITC Proceeding at 198-230 (stating Plaintiff's, Defendant Shenzhou's, and ITC staffs' respective positions on infringement due to different determinations of mole percent). In the ITC Proceeding, the mole percent term was not construed, and, as a result, Kaneka failed to carry its burden of proof with regard to at least one "key dispute": the mole percent of reduced CoQ_{10}.[3] This difficulty in the ITC makes it clear that Kaneka's position, that no construction is necessary, leaves the claim so

[3] Plaintiff acknowledges that the determination of non-infringement in the ITC Proceeding turned on the method of testing used to determine the mole percent. Plaintiff's tests showed above 70 mole percent of reduced CoQ_{10}; Defendants' tests showed below 70 mole percent. Transcript of May 7, 2013 Status Conference at 5:16-6:20. Each party argued that the other party's method of testing was erroneous. *Id*. The ITC judge therefore concluded that Plaintiff did not meet its burden of proof as to the 70 mole percent claim limitation. *Id*.

ambiguous that a person of ordinary skill in the art at the time of the invention could not understand it.

Fortunately, the specification resolves this ambiguity. The '340 Patent teaches a method of measuring the amount of reduced CoQ_{10} and describes an example in which this method is applied. According to the specification:

> The above-mentioned measurement method is provided for the obtained result to reflect the reduced coenzyme Q_{10} content and the ratio of reduced coenzyme Q_{10} among the entire coenzymes Q_{10} as accurate as possible, and to standardize the content and the ratio of reduced coenzyme Q_{10}, which can be guaranteed at the minimum. This method has been demonstrated, by several experimentations performed by the present inventors, easy and suitable to be carried out.

Id. at 5:36-43 (emphasis added). Where a claim term is ambiguous, guidance in resolving the ambiguity can come from the intrinsic record. *See, e.g.*, *Biosig Instruments, Inc. v. Nautilus, Inc.*, 715 F.3d 891, 898 (Fed. Cir. 2013) (considering intrinsic evidence, including the patent specification, in applying the principles of claim construction and indefiniteness). The specification provides a "demonstrated" method to "standardize" the determination of the ratio of reduced CoQ_{10}, and therein addresses and resolves the ambiguity of the mole percent term.

The Court finds that **"culturing reduced coenzyme Q_{10} producing microorganisms . . . to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10}"** means **"culturing reduced coenzyme Q_{10} producing microorganisms to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10} at a time prior to the extraction, oxidation, or disruption steps and as determined by the assay described at col. 5, line 8 to line 43, and Example 1 of the '340 patent."**

//

//

D. "oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" and **"oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}"**

Claim Nos.	Claim Term	Plaintiff's Construction	Defendants' Construction
1, 22	**"oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}"**	No construction necessary. Alternatively: "increasing the rate at which the reduced coenzyme Q_{10} converts to oxidized coenzyme Q_{10}"	"actively converting all or substantially all of the reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a step before beginning the extraction step"
11, 33	**"oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}"**	No construction necessary. Alternatively: "increasing the rate at which the reduced coenzyme Q_{10} converts to oxidized coenzyme Q_{10}"	"actively converting all or substantially all of the extracted reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a separate step after the extraction step has been performed"

Plaintiff argues that the term "oxidizing . . . reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" does not require construction. Defendants argue that the oxidation must occur either before or after the extraction step, depending upon the order of the steps in the claim. Defendants further argue that the term oxidizing . . . reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" should be construed to require active conversion of all or substantially all of the reduced CoQ_{10}.

The same argument with respect to the order of steps was addressed in the ITC Proceeding. ITC Proceeding at 27-28. The Court adopts the reasoning presented in

the ITC Proceeding with respect to the claim construction of the order of steps, including the "oxidation" step. *See id*. The Court has again drawn the same conclusions using the same intrinsic evidence and substantially the same extrinsic evidence presented in that case.

Plaintiff's argument that the term "oxidizing" does not require construction is undermined by its own insistence that oxidation and reduction occur naturally during each step of the production process. In contrast, the asserted claims are directed to methods where oxidation is performed on a product from a prior step to create a new compound. The specification provides examples of the oxidizing step using an oxidizing agent, which supports the understanding that the oxidation step was in fact a separate step requiring active conversion of the reduced CoQ_{10} into oxidized CoQ_{10}. The '340 Patent at 17:8-42, 20:60-21:42.

Plaintiff's alternative construction, "increasing the rate" of conversion, does not help clarify the meaning of "oxidize." Without a baseline reference for comparison, a person of skill in the art cannot know whether a rate of conversion is increased. Plaintiff relies on the Moreira Report to support its argument that one of ordinary skill in the art would understand the term "oxidizing" to mean "increasing the rate" of conversion to oxidized CoQ_{10}., but, regardless of the Moreira Report, Plaintiff's proposed construction is too vague to adopt.

On the other hand, Defendants' proposed construction includes the type of oxidation described in the '340 Patent as well as the meanings suggested by the extrinsic evidence, including the Moreira Report. The structure of the claims and the examples in the specification support the construction of "oxidation" as an active process and as converting all or most of the CoQ_{10} into an oxidized form.

The Court finds that **"oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}"** means **"actively converting all or substantially all of the reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a step before beginning the extraction step."**

The Court further finds that **"oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}"** means **"actively converting all or substantially all of the extracted reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a separate step after the extraction step has been performed."**

V. Conclusion

Claim Term	Claim Construction
"inert gas atmosphere"	"a gas atmosphere that is free or substantially free of oxygen and reactive gases"
"sealed tank"	"a tank that is closed to prevent the entry or exit of materials"
"culturing reduced coenzyme Q_{10} producing microorganisms . . . to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10}"	"culturing reduced coenzyme Q_{10} producing microorganisms to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10} at a time prior to the extraction, oxidation, or disruption steps and as determined by the assay described at col. 5, line 8 to line 43, and Example 1 of the '340 Patent."
"oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}"	"actively converting all or substantially all of the reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a step before beginning the extraction step"
"oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}"	"actively converting all or substantially all of the extracted reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a separate step after the extraction step has been performed"

//

//

//

IT IS SO ORDERED.

DATED: July 24, 2013

Hon. Mariana R. Pfaelzer
United States District Judge

Link: 188

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA
WESTERN DIVISION

KANEKA CORPORATION,

Plaintiff,

v.

XIAMEN KINGDOMWAY GROUP CO., PACIFIC RAINBOW INTERNATIONAL INC., MITSUBISHI GAS CHEMICAL COMPANY, INC., MAYPRO INDUSTRIES, INC., and SHENZHOU BIOLOGY & TECHNOLOGY CO., LTD.,

Defendants.

Case No. 2:11-cv-02389-MRP-SS

Order Granting in Part Defendants Xiamen Kingdomway Group Co. and Pacific Rainbow International Inc.'s Motion for Summary Judgment of Noninfringement of U.S. Patent No. 7,910,340 and Denying Kaneka Corporation's Motion to Suspend Response Under FED. R. CIV. PROC. 56(d)

UNDER SEAL

I. Introduction

Plaintiff Kaneka Corporation ("Kaneka") has asserted U.S. Patent No. 7,910,340 (the '340 Patent) against defendants Xiamen Kingdomway Group Co. ("XKGC"), Pacific Rainbow International Inc.("PRI"), Shenzhou Biology & Technology Co., Ltd., and Maypro Industries, Inc. (collectively "Defendants"). The '340 Patent relates to processes for producing the chemical coenzyme Q_{10}

("CoQ_{10}") on an industrial scale. XKGC and PRI move for summary judgment of noninfringement as to XKGC's process for manufacturing CoQ_{10}. In response, Kaneka moves to suspend its deadline to respond under FED. R. CIV. P. 56(d). Having read and considered all of the briefs and arguments of the parties, the Court concludes that XKGC's process for manufacturing CoQ_{10} does not infringe the '340 Patent. The Court **DENIES** Kaneka's Motion to Suspend Response. The Court **GRANTS IN PART** XKGC and PRI's Motion for Summary Judgment of Noninfringement.

II. Procedural History

Plaintiff filed its complaint for patent infringement in this Court on March 22, 2011. Complaint (Doc. No. 1). According to the complaint, XKGC allegedly infringes the '340 Patent by manufacturing CoQ_{10} using the patented process, and PRI allegedly infringes based upon its importation and sale of XKGC's CoQ_{10} product. *Id*., ¶¶ 16–17. On June 17, 2011, Plaintiff filed a complaint alleging infringement of the '340 Patent against Defendants in the International Trade Commission. *See* Certain Coenzyme Q10 Products and Methods of Making Same, Inv. No. 333-TA-790, USITC Pub. 4407 (Sept. 27, 2012) (Final) ("ITC Proceeding"). The Court granted the parties' motion to stay this case. Order re Stipulation to Stay District Court Action Pending ITC Investigation (Doc. No. 59). The stay was lifted on February 7, 2013 after the conclusion of the ITC Proceeding. Status Report (Doc. No. 70). In the parties' Joint Rule 26(f) Report, the parties noted that "[m]uch of [the anticipated] discovery (except for discovery on damages) ha[d] already occurred" during the ITC Proceeding. (Doc. No. 92.) The parties thereafter stipulated that all discovery taken during the ITC Proceeding may be used as if the discovery were taken in this case, including all confidential business information. Stipulated Protective Order (Doc. No. 97). This Court

//

//

issued a Claim Construction Order construing four terms at issue in the case on July 24, 2013. (Doc. No. 155.)[1]

III. Legal Standard

A grant of summary judgment is appropriate "if the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." FED. R. CIV. P. 56(a). The parties may use "the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any," to show the existence or absence of a genuine dispute as to any material fact. FED. R. CIV. P. 56(c). The Court must draw all reasonable inferences from the evidence in favor of the non-movant, *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 255 (1986), and may grant summary judgment when it is apparent that only one conclusion as to infringement could be reached by a reasonable jury, *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 540 (Fed. Cir. 1998).

The Court cannot grant summary judgment if the dispute about a material fact is genuine such that a reasonable jury could return a verdict for the nonmoving party. *Id.* Faced with a properly supported summary judgment motion, the nonmoving party may not rest upon mere allegations or denials of its pleading but must set forth specific facts showing a genuine issue for trial. *Id.* "Where the record taken as a whole could not lead a rational trier of fact to find for the nonmoving party, there is no genuine issue for trial." *Matsushita Elec. Indus. Co. v. Zenith Radio Corp.*, 475 U.S. 574, 587 (1986).

The legal standard for infringement is stringent and requires that the Court find that the accused product meet every claim limitation in the asserted claim. This comparison "requires a factual determination that every claim limitation or its equivalent is found in the accused device." *Int'l Rectifier Corp. v. IXYS Corp.*, 361

[1] Kaneka indicates that discovery in this case did not open until after the Court issued the Claim Construction Order by citing to statements made by the Court on the issue of bifurcating infringement and damages discovery. *See* Transcript for Proceeds Held on May 7, 2013 at 18:10–21:20 (Doc. No. 110). While discovery on damages has not opened in this case, Kaneka's assertion that discovery on infringement was not open is incorrect.

F.3d 1363, 1369 (Fed. Cir. 2004). Consequently, the patentee's failure to show the presence of any single claim limitation or its equivalent in the accused products allows the Court to grant summary judgment. "Summary judgment of noninfringement is . . . appropriate where the patent owner's proof is deficient in meeting an essential part of the legal standard for infringement, because such failure will render all other facts immaterial." *TechSearch, L.L.C. v. Intel Corp.*, 286 F.3d 1360, 1369 (Fed. Cir. 2002) (citation omitted). If there is no infringement of an independent claim, then there can be no infringement of any claim depending from the independent claim as a matter of law. *See Voter Verified, Inc. v. Premier Election Solutions, Inc.*, 698 F.3d 1374, 1383 (Fed. Cir. 2012).

If a moving party files a motion for summary judgment before the nonmoving party has had a realistic opportunity to pursue discovery relating to its theory of the case, the Court may grant a motion to suspend the deadline to respond to the motion for summary judgment until adequate discovery is taken. FED. R. CIV. P. 56(c); *see Burlington N. Santa Fe R. Co. v. Assiniboine & Sioux Tribes of Fort Peck Reservation*, 323 F.3d 767, 773 (9th Cir. 2003). If the incomplete discovery is essential to the non-moving party's theory of the case, the Court must suspend the deadline to respond. *Metabolife Int'l, Inc. v. Wornick*, 264 F.3d 832, 846 (9th Cir. 2001). In seeking relief under Rule 56(d), the nonmoving party "must make clear what information is sought and how it would preclude summary judgment." *Margolis v. Ryan*, 140 F.3d 850, 853 (9th Cir.1998) (quotations omitted). In addition, the nonmoving party must have been diligent in pursuing discovery in the past. *Cal. Union Ins. Co. v. Am. Diversified Sav. Bank*, 914 F.2d 1271, 1278 (9th Cir. 1990) (citations omitted).

//

//

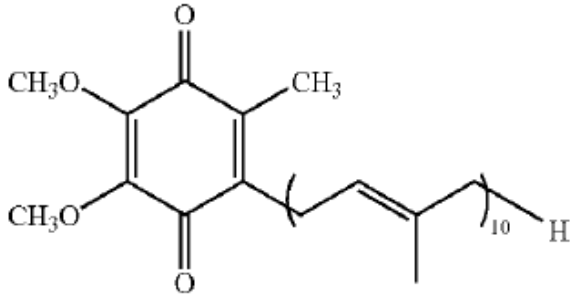
//

IV. Technical Background

A. The Asserted Claims of the '340 Patent

Kaneka asserts claims 1, 8–9, 11, 19–20, 22, 30, 32–33, 43, and 45 of the '340 Patent. The asserted claims are directed to processes for producing oxidized CoQ_{10} on an industrial scale. The CoQ_{10} molecule occurs naturally in the membranes of animal cells where it is used to produce adenosine triphosphate to aid in cellular respiration. CoQ_{10} exists in three forms: oxidized, semi-oxidized, and reduced. Each of the three forms of CoQ_{10} has a distinct molecular structure. The claims of the '340 Patent are directed to processes for producing the reduced form of CoQ_{10} at a provided mole percentage and oxidizing the reduced CoQ_{10}.

Claim 11 provides an example of the asserted independent claims and reads as follows:

> 11. A process for producing on an industrial scale the oxidized coenzyme Q_{10} represented by the following formula:
>
> 
>
>
> which comprises culturing reduced coenzyme Q_{10}-producing microorganisms in a culture medium containing a carbon source, a nitrogen source, a phosphorus source and a micronutrient to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10},
>
> extracting the reduced coenzyme Q_{10} by an organic solvent under an inert gas atmosphere, and

//

> oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}.

The '340 Patent at 24:50–25:6. Independent claim 1 provides an additional disrupting step, and describes the oxidizing and extracting steps as follows:

> oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10} and then extracting the oxidized coenzyme Q_{10} by an organic solvent under an inert gas atmosphere.

Id. at 23:56–24:25. Independent claims 22 and 33 differ from claims 1 and 11 respectively in that they require that the extracting step occur "in a sealed tank" rather than under an inert gas atmosphere. *Id*. at 25:32-54, 26:13-36.

In its Claim Construction Order, the Court construed the following five terms:

Claim Term	Claim Construction
"inert gas atmosphere"	"a gas atmosphere that is free or substantially free of oxygen and reactive gases"
"sealed tank"	"a tank that is closed to prevent the entry or exit of materials"
"culturing reduced coenzyme Q_{10} producing microorganisms . . . to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10}"	"culturing reduced coenzyme Q_{10} producing microorganisms to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10} at a time prior to the extraction, oxidation, or disruption steps and as determined by the assay described at col. 5, line 8 to line 43, and Example 1 of the '340 Patent."
"oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}"	"actively converting all or substantially all of the reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a

Confidential Material Redacted

Claim Term	Claim Construction
	step before beginning the extraction step"
"oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}"	"actively converting all or substantially all of the extracted reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a separate step after the extraction step has been performed"

[redacted]

V. Motion to Suspend Deadline to Respond

The request for a continuance in response to a motion for summary judgment is an important tool to allow litigants full access to the discovery needed to properly present each side of the case. In order to prevent litigants from abusing the Rule 56(d) tool, the party requesting a continuance may not simply argue that additional discovery is required; the requesting party must show specific facts to be obtained by additional discovery that will raise an issue of material fact. *See Continental Maritime v. Pacific Coast Metal Trades*, 817 F.2d 1391, 1395 (9th Cir. 1987).

[redacted]

Kaneka's request 3, which simply states that Kaneka needs discovery on a particular claim limitation, describes a general area for discovery, not specific facts to be obtained by discovery. First, this request is too general to allow a continuance under Rule 56(d). Discovery on or about a claim limitation identifies

an issue in the case, not a specific fact to be investigated. Second, Kaneka already has access to sufficient discovery in this critical area. [redacted] A Rule 56(d) motion is not an appropriate remedy merely because the facts revealed by the discovery in the ITC Proceeding do not support Kaneka's infringement theory. [redacted]

[2] Kaneka's request 4 is sufficiently specific if combined with Kaneka's clarifying statements that it seeks discovery "regarding whether the drying procedure including the use of suction fans, blast fans, air-flow drying units, and cooling fans ducts blowing compressed air through the biomass would be considered . . . active oxidation" by a person of ordinary skill in the art. Kaneka's Br. at 10.

Confidential Material Redacted

[redacted]

//

Confidential Material Redacted

[redacted]

VI. Motion for Summary Judgment

In order for XKGC's process to infringe the '340 Patent, the process must meet each claim limitation of an asserted claim. [redacted]

A. "inert gas atmosphere"

Claims 1 and 11 include claim limitations that require extraction to occur under an inert gas atmosphere. Claim 1 requires "extracting the oxidized coenzyme Q_{10} by an organic solvent under an inert gas atmosphere," and claim 11 requires "extracting the reduced coenzyme Q_{10} by an organic solvent under an inert gas atmosphere." In its Claim Construction Order, the Court found that "inert gas atmosphere" meant "a gas atmosphere that is free or substantially free of oxygen and reactive gases." The Court noted that it had drawn the same conclusions from the same evidence presented in the ITC Proceeding in reaching its construction.

[redacted]

[redacted]

B. "sealed tank"

Claims 22 and 33 include claim limitations that require extraction to occur in a sealed tank. Claim 22 requires "extracting the oxidized coenzyme Q_{10} by an organic solvent in a sealed tank," and claim 33 requires "extracting the reduced coenzyme Q_{10} by an organic solvent in a sealed tank." In its Claim Construction Order, the Court found that "sealed tank" meant "a tank that is closed to prevent the entry or exit of materials." The Court again noted that it had drawn the same conclusions from the same evidence presented in the ITC Proceeding in reaching its construction.

[redacted]

[redacted]

C. "oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" and "oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}"

Claims 1, 11, 22, and 33 include claim limitations that require an oxidation step. Claims 1 and 22 require "oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}," and claims 11 and 33 require "oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}." In its Claim Construction Order, the Court found that the oxidation term in claims 1 and 22 meant "actively converting all or substantially all of the reduced [Co]Q_{10} obtained from the disruption step to oxidized [Co]Q_{10} in a step before beginning the extraction step."

The Court further found that the oxidation term in claims 11 and 33 meant "actively converting all or substantially all of the extracted reduced [Co]Q_{10} obtained from the disruption step to oxidized [Co]Q_{10} in a separate step after the extraction step has been performed."

Under the Court's constructions, several limitations must be met during the oxidation step of the patented processes. First, the conversion from reduced CoQ_{10} to oxidized CoQ_{10} must be an active, not a passive, process. Second, all or substantially all of the reduced CoQ_{10} must be converted during the oxidation step. Third, the oxidation step must occur separately from the culturing, disruption, and extraction steps. Fourth, the oxidation step must occur either before the extraction step for Claims 1 and 22 or after the extraction step for Claims 11 and 33.

[redacted]

Confidential Material Redacted

[redacted]

VII. Conclusion

The Court **DENIES** Kaneka's Motion to Suspend Response [redacted]

The Court **GRANTS IN PART** XKGC and PRI's Motion for Summary Judgment of Noninfringement because the Court finds that no genuine issue of material fact

exists as to whether XKGC's process infringes every element of the asserted claims of the '340 Patent.

IT IS SO ORDERED.

DATED: December 6, 2013

Hon. Mariana R. Pfaelzer
United States District Judge

Links: 158, 176

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA
WESTERN DIVISION

KANEKA CORPORATION,

Plaintiff,

v.

XIAMEN KINGDOMWAY GROUP CO., PACIFIC RAINBOW INTERNATIONAL INC., MITSUBISHI GAS CHEMICAL COMPANY, INC., MAYPRO INDUSTRIES, INC., and SHENZHOU BIOLOGY & TECHNOLOGY CO., LTD.,

Defendants.

Case No. 2:11-cv-02389-MRP-SS

Order Granting in Part Defendant Shenzhou Biology & Technology Co., Ltd.'s Motion for Summary Judgment of Noninfringement of U.S. Patent No. 7,910,340 and Denying Kaneka Corporation's Motion to Suspend Response Under FED. R. CIV. PROC. 56(d)

UNDER SEAL

I. Introduction

Plaintiff Kaneka Corporation ("Kaneka") has asserted U.S. Patent No. 7,910,340 (the '340 Patent) against defendants Shenzhou Biology & Technology Co., Ltd. ("Shenzhou"), Xiamen Kingdomway Group Co., Pacific Rainbow International Inc., and Maypro Industries, Inc. (collectively "Defendants"). The '340 Patent relates to processes for producing the chemical coenzyme Q_{10}

("CoQ_{10}") on an industrial scale. Shenzhou moves for summary judgment of noninfringement as to Shenzhou's process for manufacturing CoQ_{10}. In response, Kaneka moves to suspend its deadline to respond under FED. R. CIV. P. 56(d). Having read and considered all of the briefs and arguments of the parties, the Court concludes that Shenzhou's process for manufacturing CoQ_{10} does not infringe the '340 Patent. The Court **DENIES** Kaneka's Motion to Suspend Response. The Court **GRANTS IN PART** Shenzhou's Motion for Summary Judgment of Noninfringement.

II. Procedural History

Plaintiff filed its complaint for patent infringement in this Court on March 22, 2011. Complaint (Doc. No. 1). On June 17, 2011, Plaintiff filed a complaint alleging infringement of the '340 Patent against Defendants in the International Trade Commission. *See* Certain Coenzyme Q10 Products and Methods of Making Same, Inv. No. 333-TA-790, USITC Pub. 4407 (Sept. 27, 2012) (Final) ("the ITC Proceeding"). The Court granted the parties' motion to stay this case. Order re Stipulation to Stay District Court Action Pending ITC Investigation (Doc. No. 59). The stay was lifted on February 7, 2013 after the conclusion of the ITC Proceeding. Status Report (Doc. No. 70). In the parties' Joint Rule 26(f) Report, the parties noted that "[m]uch of [the anticipated] discovery (except for discovery on damages) ha[d] already occurred" during the ITC Proceeding. (Doc. No. 92.) The parties thereafter stipulated that all discovery taken during the ITC Proceeding may be used as if the discovery were taken in this case, including all confidential business information. Stipulated Protective Order (Doc. No. 97). This Court issued a Claim Construction Order construing four terms at issue in the case on July 24, 2013. (Doc. No. 155.)[1]

[1] Kaneka indicates that discovery in this case did not open until after the Court issued the Claim Construction Order by citing to statements made by the Court on the issue of bifurcating infringement and damages discovery. *See* Transcript for Proceeds Held on May 7, 2013 at 18:10–21:20 (Doc. No. 110). While discovery on damages has not opened in this case, Kaneka's assertion that discovery on infringement was not open is incorrect.

III. Legal Standard

A grant of summary judgment is appropriate "if the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." FED. R. CIV. P. 56(a). The parties may use "the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any," to show the existence or absence of a genuine dispute as to any material fact. FED. R. CIV. P. 56(c). The Court must draw all reasonable inferences from the evidence in favor of the non-movant, *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 255 (1986), and may grant summary judgment when it is apparent that only one conclusion as to infringement could be reached by a reasonable jury, *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 540 (Fed. Cir. 1998).

The Court cannot grant summary judgment if the dispute about a material fact is genuine such that a reasonable jury could return a verdict for the nonmoving party. *Id.* Faced with a properly supported summary judgment motion, the nonmoving party may not rest upon mere allegations or denials of its pleading but must set forth specific facts showing a genuine issue for trial. *Id.* "Where the record taken as a whole could not lead a rational trier of fact to find for the nonmoving party, there is no genuine issue for trial." *Matsushita Elec. Indus. Co. v. Zenith Radio Corp.*, 475 U.S. 574, 587 (1986).

The legal standard for infringement is stringent and requires that the Court find that the accused product meet every claim limitation in the asserted claim. This comparison "requires a factual determination that every claim limitation or its equivalent is found in the accused device." *Int'l Rectifier Corp. v. IXYS Corp.*, 361 F.3d 1363, 1369 (Fed. Cir. 2004). Consequently, the patentee's failure to show the presence of any single claim limitation or its equivalent in the accused products allows the Court to grant summary judgment. "Summary judgment of noninfringement is . . . appropriate where the patent owner's proof is deficient in meeting an essential part of the legal standard for infringement, because such

failure will render all other facts immaterial." *TechSearch, L.L.C. v. Intel Corp.*, 286 F.3d 1360, 1369 (Fed. Cir. 2002) (citation omitted). If there is no infringement of an independent claim, then there can be no infringement of any claim depending from the independent claim as a matter of law. *See Voter Verified, Inc. v. Premier Election Solutions, Inc.*, 698 F.3d 1374, 1383 (Fed. Cir. 2012).

If a moving party files a motion for summary judgment before the nonmoving party has had a realistic opportunity to pursue discovery relating to its theory of the case, the Court may grant a motion to suspend the deadline to respond to the motion for summary judgment until adequate discovery is taken. FED. R. CIV. P. 56(c); *see Burlington N. Santa Fe R. Co. v. Assiniboine & Sioux Tribes of Fort Peck Reservation*, 323 F.3d 767, 773 (9th Cir. 2003). If the incomplete discovery is essential to the non-moving party's theory of the case, the Court must suspend the deadline to respond. *Metabolife Int'l, Inc. v. Wornick*, 264 F.3d 832, 846 (9th Cir. 2001). In seeking relief under Rule 56(d), the nonmoving party "must make clear what information is sought and how it would preclude summary judgment." *Margolis v. Ryan*, 140 F.3d 850, 853 (9th Cir.1998) (quotations omitted). In addition, the nonmoving party must have been diligent in pursuing discovery in the past. *Cal. Union Ins. Co. v. Am. Diversified Sav. Bank*, 914 F.2d 1271, 1278 (9th Cir. 1990) (citations omitted).

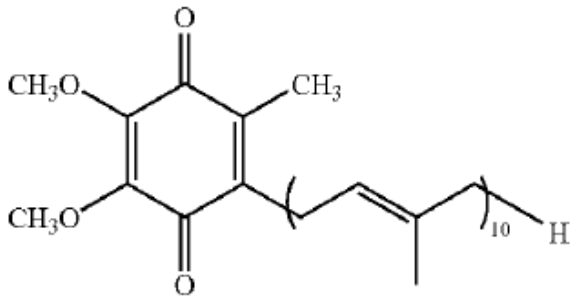
IV. Technical Background

A. The Asserted Claims of the '340 Patent

Kaneka asserts claims 1, 8–9, 11, 19–20, 22, 30, 32–33, 43, and 45 of the '340 Patent. The asserted claims are directed to processes for producing oxidized CoQ_{10} on an industrial scale. The CoQ_{10} molecule occurs naturally in the membranes of animal cells where it is used to produce adenosine triphosphate to aid in cellular respiration. CoQ_{10} exists in three forms: oxidized, semi-oxidized, and reduced. Each of the three forms of CoQ_{10} has a distinct molecular structure. The claims of

the ’340 Patent are directed to processes for producing the reduced form of CoQ_{10} at a provided mole percentage and oxidizing the reduced CoQ_{10}.

Claim 11 provides an example of the asserted independent claims and reads as follows:

> 11. A process for producing on an industrial scale the oxidized coenzyme Q_{10} represented by the following formula:
>
> 
>
>
> which comprises culturing reduced coenzyme Q_{10}-producing microorganisms in a culture medium containing a carbon source, a nitrogen source, a phosphorus source and a micronutrient to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10},
>
> extracting the reduced coenzyme Q_{10} by an organic solvent under an inert gas atmosphere, and
>
> oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}.

The ’340 Patent at 24:50–25:6. Independent claim 1 provides an additional disrupting step, and describes the oxidizing and extracting steps as follows:

> oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10} and then extracting the oxidized coenzyme Q_{10} by an organic solvent under an inert gas atmosphere.

//

//

Id. at 23:56–24:25. Independent claims 22 and 33 differ from claims 1 and 11 respectively in that they require that the extracting step occur "in a sealed tank" rather than under an inert gas atmosphere. *Id*. at 25:32-54, 26:13-36.

In its Claim Construction Order, the Court construed the following five terms:

Claim Term	Claim Construction
"inert gas atmosphere"	"a gas atmosphere that is free or substantially free of oxygen and reactive gases"
"sealed tank"	"a tank that is closed to prevent the entry or exit of materials"
"culturing reduced coenzyme Q_{10} producing microorganisms . . . to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10}"	"culturing reduced coenzyme Q_{10} producing microorganisms to obtain microbial cells containing reduced coenzyme Q_{10} at a ratio of not less than 70 mole % among the entire coenzymes Q_{10} at a time prior to the extraction, oxidation, or disruption steps and as determined by the assay described at col. 5, line 8 to line 43, and Example 1 of the '340 Patent."
"oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}"	"actively converting all or substantially all of the reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a step before beginning the extraction step"
"oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}"	"actively converting all or substantially all of the extracted reduced coenzyme Q_{10} obtained from the disruption step to oxidized coenzyme Q_{10} in a separate step after the extraction step has been performed"

Confidential Material Redacted

B. Shenzhou's Accused Process for Producing CoQ_{10}

[redacted]

[redacted]

Confidential Material Redacted

[redacted]d

[redacted]

V. Motion to Suspend Deadline to Respond

The request for a continuance in response to a motion for summary judgment is an important tool to allow litigants full access to the discovery needed to properly present each side of the case. In order to prevent litigants from abusing the Rule 56(d) tool, the party requesting a continuance may not simply argue that additional discovery is required; the requesting party must show specific facts to be obtained by additional discovery that will raise an issue of material fact. *See Continental Maritime v. Pacific Coast Metal Trades*, 817 F.2d 1391, 1395 (9th Cir. 1987). According to Kaneka's counsel, Kaneka needs critical discovery on:

[redacted]

Declaration of Robert M. Bowick in Support of Plaintiff's Motion to Suspend Response Deadline Under Fed. R. Civ. Pro. 56(d), Ex. 2 at 2–3 (Doc. No. 178).

Kaneka's requests describe general areas for discovery, not specific facts to be obtained by discovery. First, these requests are too general to allow a continuance under Rule 56(d). Discovery on or about a claim limitation identifies an issue in the case, not a specific fact to be investigated. Second, Kaneka already has access to sufficient discovery in these critical areas. [redacted]

[redacted]

Kaneka's "mere hope that further evidence may develop . . . is an insufficient basis for a continuance." *Continental Maritime*, 817 F.2d at 1395. A Rule 56(d) motion is not an appropriate remedy merely because the facts revealed by the discovery in the ITC Proceeding do not support Kaneka's infringement theory. Kaneka's request for a continuance pending discovery related to the inert gas atmosphere, the extraction tank exhaust system, and the oxidation step is therefore denied.

[redacted]

Kaneka correctly argues that under the Court's claim construction, the discovery taken on the mole percent ratio limitation in the ITC Proceeding is no longer relevant or helpful to Kaneka's case. Indeed, Shenzhou's argument for summary judgment on this limitation is primarily directed to Kaneka's lack of proof of infringement. Since Kaneka has had no discovery on this claim limitation,

Shenzhou's motion is premature. Although Kaneka's affidavit provides only a general request and not specific facts, [redacted]

VI. Motion for Summary Judgment

In order for Shenzhou's process to infringe the '340 Patent, the process must meet each claim limitation of an asserted claim. Therefore, although the Court would be inclined to grant Kaneka's motion for a continuance as to the mole percent ratio limitation, Shenzhou's motion for summary judgment is still a timely, dispositive motion with respect to the remaining three claim terms construed in the Claim Construction Order.

A. "inert gas atmosphere"

Claims 1 and 11 include claim limitations that require extraction to occur under an inert gas atmosphere. Claim 1 requires "extracting the oxidized coenzyme Q_{10} by an organic solvent under an inert gas atmosphere," and claim 11 requires "extracting the reduced coenzyme Q_{10} by an organic solvent under an inert gas atmosphere." In its Claim Construction Order, the Court found that "inert gas atmosphere" meant "a gas atmosphere that is free or substantially free of oxygen and reactive gases." The Court noted that it had drawn the same conclusions from the same evidence presented in the ITC Proceeding in reaching its construction.

//

Confidential Material Redacted

[redacted]

Kaneka uses its opposition to the summary judgment motion to rehash its argument from claim construction. The Court rejected Kaneka's proposition to construe the term "inert gas atmosphere" solely in light of safety considerations.

[redacted]

[redacted]

B. "sealed tank"

Claims 22 and 33 include claim limitations that require extraction to occur in a sealed tank. Claim 22 requires "extracting the oxidized coenzyme Q_{10} by an organic solvent in a sealed tank," and claim 33 requires "extracting the reduced coenzyme Q_{10} by an organic solvent in a sealed tank." In its Claim Construction Order, the Court found that "sealed tank" meant "a tank that is closed to prevent the entry or exit of materials." The Court again noted that it had drawn the same conclusions from the same evidence presented in the ITC Proceeding in reaching its construction.

[redacted]

[redacted] Where, as here, a claim limitation is added by amendment to overcome an examiner's rejection, Kaneka must show that a person of ordinary skill in the art would not have reasonably been expected to draft a claim that could have encompassed the equivalent. *Festo Corp. v. Shoketsu Kinoku Kogyo Kabsuhiki Co.*, 535 U.S. 722, 740–41 (2002). Kaneka has made no showing that a person of ordinary skill in the art at the time of the '340 Patent could not have been expected to draft a claim to encompass an exhaust or relief valve on a sealed tank for industrial chemical extraction.

[redacted]

C. "oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}" and **"oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}"**

Claims 1, 11, 22, and 33 include claim limitations that require an oxidation step. Claims 1 and 22 require "oxidizing thus-obtained reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}," and claims 11 and 33 require "oxidizing the extracted reduced coenzyme Q_{10} to oxidized coenzyme Q_{10}." In its Claim Construction Order, the Court found that the oxidation term in claims 1 and 22 meant "actively converting all or substantially all of the reduced [Co]Q_{10} obtained from the disruption step to oxidized [Co]Q_{10} in a step before beginning the extraction step." The Court further found that the oxidation term in claims 11 and 33 meant "actively converting all or substantially all of the extracted reduced [Co]Q_{10} obtained from the disruption step to oxidized [Co]Q_{10} in a separate step after the extraction step has been performed."

//

Confidential Material Redacted

Under the Court's constructions, several limitations must be met during the oxidation step of the patented processes. First, the conversion from reduced CoQ_{10} to oxidized CoQ_{10} must be an active, not a passive, process. Second, all or substantially all of the reduced CoQ_{10} must be converted during the oxidation step. Third, the oxidation step must occur separately from the culturing, disruption, and extraction steps. Fourth, the oxidation step must occur either before the extraction step for Claims 1 and 22 or after the extraction step for Claims 11 and 33. According to Shenzhou, Kaneka has failed to show that each of these limitations is met.

[redacted]

Confidential Material Redacted

[redacted]

VII. Conclusion

The Court **DENIES** Kaneka's Motion to Suspend Response with respect to the inert gas atmosphere, sealed tank, and oxidation step claim elements. Although the Court is inclined to grant Kaneka's Motion to Suspend Response with respect to the mole percent ratio claim element, the Court **DENIES** Kaneka's motion with

respect to the mole percent ratio claim element because additional discovery would be moot in light of the Court's finding of noninfringement of other claim elements. The Court **GRANTS IN PART** Shenzhou's Motion for Summary Judgment of Noninfringement because the Court finds that no genuine issue of material fact exists as to whether Shenzhou's process infringes every element of the asserted claims of the '340 Patent.

IT IS SO ORDERED.

DATED: December 6, 2013

Hon. Mariana R. Pfaelzer
United States District Judge

United States Court of Appeals
for the Federal Circuit

Kaneka Corporation v. Zhejiang Medicine Co., Ltd., 2014-1373, -1399

CERTIFICATE OF SERVICE

I, Robyn Cocho, being duly sworn according to law and being over the age of 18, upon my oath depose and say that:

Counsel Press was retained by CARTER LEDYARD & MILBURN LLP, Attorneys for Appellant to print this document. I am an employee of Counsel Press.

On **June 19, 2014,** counsel authorized me to electronically file the foregoing corrected **Brief for Plaintiff-Appellant (confidential and non-confidential versions)** with the Clerk of Court using the CM/ECF System, which will serve via e-mail notice of such filing to all counsel registered as CM/ECF users, including any of the following:

Timothy P. Walker
(Principal Counsel)
Harold H. Davis, Jr.
Jas S. Dhillon
K&L Gates LLP
Four Embarcadero Center
Suite 1200
San Francisco, CA 94111
415-882-8200
timothy.walker@klgates.com
harold.davis@klgates.com
jas.dhillon@klgates.com

Matthew B. O'Hanlon
K&L Gates LLP
10100 Santa Monica Boulevard
Los Angeles, CA 90067
310-552-5548
matthew.ohanlon@klgates.com

Counsel for Defendants-Appellee
Shenzhou Biology & Technology Co., Ltd.

Reece W. Nienstadt
(Principal Counsel)
Lei Mei
Xiang Long
Mei & Mark LLP
P.O. Box 65981
Washington, DC 20035
888-860-5678
rnienstadt@meimark.com
xlong@meimark.com
mei@meimark.com,

Counsel for Defendants-Appellees
Xiamen Kingdomway Group Company,
and Pacific Rainbow International Inc.

Copies will also be served via e-mail to the above counsel, and sent Express Mail to the above principal counsel on this same date.

Upon acceptance by the Court of the e-filed document, six paper copies will be filed with the Court, via Federal Express, within the time provided in the Court's rules. The brief was originally filed and serve on June 3, 2014.

June 19, 2014

/s/ Robyn Cocho
Counsel Press

CERTIFICATE OF COMPLIANCE WITH TYPE-VOLUME LIMITATION, TYPEFACE REQUIREMENTS AND TYPE STYLE REQUIREMENTS

1. This brief complies with the type-volume limitation of Federal Rule of Appellate Procedure 32(a)(7)(B).

__X__ The brief contains __13,712__ words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(a)(7)(B)(iii),or

____ The brief uses a monospaced typeface and contains _____ lines of text, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(a)(7)(B)(iii).

2. This brief complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type style requirements of Federal Rule of Appellate Procedure 32(a)(6).

__X__ The brief has been prepared in a proportionally spaced typeface using MS Word 2013 in a 14 point Times New Roman font or

____ The brief has been prepared in a monospaced typeface using _____ _____in a ___ characters per inch_____ font.

June 3, 2014
Date

/s/ Keith D. Nowak
Keith D. Nowak

Counsel for Plaintiff-Appellant
Kaneka Corporation